# THE BRACHIAL NEUROPATHIES

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Gowers (1899) considered that inflammation of the brachial peripheral nerves often began as a " perineuritis ", or inflammation of the sheaths of the nerves, which might spread from a neighbouring " fibrositic " process in the fascial planes and intramuscular septa at the base of the neck and shoulder. Occasional cases were seen in which trauma or the pressure of new growths on the plexus was responsible, but in the majority no focal lesion could be demonstrated, and gout and rheumatism were thought to be important predisposing causes. Gowers (1899) held that the mobility of the parts in which the brachial plexus lay must be important in maintaining the pain, and he recommended that " securing for the part as perfect rest as possible " should be the first aim in treatment.

Since the beginning of the present century there has been a surprising series of new methods of approaching this problem. Early in the century attention was focused on irritation of the lower components of the brachial plexus as they passed from the neck to the axilla:

Firstly, the radiologically obvious anomaly of a cervical rib was sought out, especially when symptoms and signs indicated a lesion of the lower components of the plexus. In these cases the common site for pain was in the distribution of C8 and T1, with paræsthesiæ or numbness in the ulnar fingers; but Adson and Coffey (1927) maintained that pain could occasionally spread over the distribution of the entire brachial plexus, and Kinnier Wilson (1940) stated that pain could involve either the ulnar or radial aspects of the forearm. Wasting of the small muscles of the hand was considered an important sign; and it is worth noting in retrospect that, in Sargent's (1921) series, these thenar cases showed poorest return of muscle bulk after removal of the cervical rib. The frequent failure of removal of the rib to cure the condition was attributed to faulty technique (Wilson 1940).

In the United States, Ochsner et al. (1935) and Naffziger and Grant (1938) introduced the idea that spasm of scalenus anticus could produce similar symptoms in the absence of a cervical rib. This was recognised clinically by tenderness over the lower third of the scalenus muscles. Reichart (1942) elaborated the concept of a vicious circle in which irritation of the medial cord of the brachial plexus as it crossed the normal first rib induced such spasm, which then further raised the thoracic inlet. Mild cases were treated with exercises to strengthen the shoulder-girdle muscles, or by lifting the shoulder with a sling, and in severe cases tenotomy of the insertion of scalenus anticus gained some measure of success. After operation the symptoms took weeks or months to resolve, whereas passive elevation of the shoulder often abolished the symptoms immediately.

Falconer and Weddell (1943) described a convincing case, in which a lesion of the lower components of the brachial plexus was ascribed to compression by a fibrous band passing from the seventh cervical vertebral transverse process to the normal first rib; and they suggested that many cases of the so-called scalenus-anticus syndrome were due to " costo-fibrous or costo-clavicular compression of the plexus " without any abnormality being visible on X-ray of the thoracic outlet. Aggravation of symptoms, and reduction of the radial pulse, by downward and backward bracing of the shoulders was regarded as an indication that the symptoms originated in this way.

Walshe (1945), impressed by the frequency of brachial neuritis in women taking up manual work during the war, concluded that " traction and compression of the lower trunk of the brachial plexus and possibly also of the subclavian artery are the essential mechanical factors underlying most, if perhaps not all, cases of acroparæsthesiæ in women, that these factors are caused by sagging of the shoulder girdle, and this, in turn, is a natural consequence of an atonic supporting musculature ". Wartenberg (1944) at the same time isolated a group under the name of " brachialgia statica paresthetica ", in which pain and paræsthesiæ, chiefly of ulnar distribution, occurred exclusively at night, which he concluded was due to irritation of the lower brachial plexus at the thoracic inlet during the muscle relaxation of sleep. Rest was found to be the essential factor in treatment in Walshe's cases, and the rearrangement of pillows and sleeping habits in Wartenberg's.

Wide radiation of pain and tenderness was thought compatible with compression of the brachial plexus at this level; in Naffziger and Grant's (1938) case-records these symptoms were often described in the neck and trapezius regions, and pain was sometimes aggravated by head movement as well as by depression of the shoulders.

## PAIN CAUSED BY PRESSURE ON NERVE-ROOTS

Meanwhile, attention was shifting to the level of the nerve-roots, and the role of the prolapsed intervetebral disc, now known to produce sciatica, was being applied to the upper limb:

In 1943 Semmes and Murphy suggested that laterally placed disc protrusions in the cervical spine might account for many cases formerly ascribed to compression at the thoracic inlet. Elliott and Kremer, in 1945, claimed that the syndrome so produced stood in clear relief from the other causes of brachial pain, and they pointed out the centrifugal radicular course of the pain, the frequency of paræsthesiæ distally in the fingers, and the accompanying focal tenderness in the muscles around the shoulder girdle which would often act as a trigger mechanism for the production of pain. While objective motor and sensory signs of a root lesion were commonly confined to the root or roots compressed, spread of pain and paræsthesiæ into neighbouring segments was thought to be due to an excitatory process within the spinal cord itself. Brain (1948) ascribed this to œdema (due to venous stasis) of the anterolateral region of the cord for some segments below the lesion. He emphasised the wide radiation of pain into muscles supplied by the compressed root, as well as into the corresponding dermatomes.

Knight (1948) showed that pain might be severe when physical signs were few or absent, and vice versa, depending on whether the involved roots were free and liable to friction or firmly fixed by the disc protrusion. Frykholm, in 1951, extended these hypothetical observations by careful experimental studies at open operation. He showed that in cases of brachial neuralgia, the dural sleeve was often thickened and rigid around the emerging nerve-roots, even where no disc protrusion could be found. This in itself was thought to be due to friction, direct trauma, congenital maldevelopment of the root pouch, or cervical osteoarthritis. Frykholm concluded that " most cases of brachalgia are probably of radicular origin ",

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and thought that many arm pains not conforming to clear root syndromes were caused by compression in the intervertebral foramen of only part of a root. Similarly, Scoville (1946) had stated that "compression of the nerve roots at the lower cervical vertebral foramina accounts for most of the diagnoses of scalenus anticus syndrome, brachial neuritis and other obscure neuralgic pains of the shoulder and arm". These papers were followed by a tendency to operate on the cervical spine in cases of brachialgia; and in 1958 two large series of operated cases were reported. Odom et al. obtained 53% of "excellent results" in 246 cases, and Scoville found 86% "markedly improved" in 400 cases. Others, however, obtained good results by the simple expedient of immobilising the neck when prolapsed-disc tissue was found or suspected (Jefferson 1951, Campbell and Phillips 1960).

Brain et al. (1952) pointed out that the typical acroparæsthesiæ seen in cases of cervical spondylosis were often worse at night and eased shortly after rising, which was a clinical feature formerly attributed to costoclavicular compression. Frykholm (1951) had found that the nerve-roots were compressed more commonly by hard bony or cartilaginous masses than by soft nuclear herniations, and Liversedge (1959) thought that osteoarthritis, cervical spondylosis, and disc herniations might all operate together at times in producing chronic radicular arm pains.

In many cases of presumed nerve-root irritation there was found to be focal tenderness or even palpable nodules in the muscles around the shoulder girdle. This had formerly been regarded as a cause of chronic arm pain sui generis; in 1927 Harris had described the therapeutic value of injecting such spots with procaine and alcohol, and Travell et al. (1942) had confirmed this, reporting that such cures might be long-lasting. In 1944, Elliott suggested that we no longer need explain this phenomenon on the basis of a primary "fibrositis" or "myalgia", and he used electromyography to indicate that it was due to active muscle spasm with a pattern of activity which suggested that the necessary impulses arose in the anterior-horn cells. Sahlgren and Sjöqvist (1944) showed that, in sciatica due to prolapsed lumbar intervertebral discs, the tender spots could be made to disappear by anæsthetising the radicular nerve. Frykholm (1951) then showed that stimulation of the *ventral* roots can produce deep boring pain in the region of the scapula and shoulder girdle which is commonly felt in the muscles themselves. The exact area of reference was difficult to determine or to correlate with the site of preoperative muscle tenderness because there was considerable overlap between one root and another. These findings all contrasted with the effect of stimulating the posterior roots, which produced sharp shock-like pain spreading distally in the limb.

### PAIN ORIGINATING FROM DISCS

More recently, Cloward (1959) has observed that dull scapular and arm pain may originate from the tissue of the cervical discs themselves:

The area of reference seems to be closely related to the part of the disc which is stimulated, midline anterior stimulation of the disc causing pain in the middle of the back, and more lateral stimulation more laterally seated pain. Pain from the C3–4 disc is referred to the upper border of trapezius, and from the C6–7 disc to the inferior angle of the scapula, with intermediate pain from the discs between. Further work (1960) with electromyography has shown that stimulation of the anterior part of the cervical disc produces involuntary spasm in the scapular muscles, and that procaine injected into the disc abolishes this. Cloward concludes that the neural pathways involve the sinuvertebral nerves.

Apart from showing a new mechanism whereby pain can arise in the region of the scapula and arm, Cloward's work is clearly of significance in showing why immobilisation of the neck can be so effective in many cases of chronic arm pain, and why operative decompression of the nerve-roots may be ineffective.

### PAIN PROVOKED PERIPHERALLY

In 1947, Brain et al. brought to light a new mechanism for the production of arm pain, showing that spontaneous compression of the median nerve under the flexor retinaculum could give pain and paræsthesiæ in the distribution of the digital branches of the median nerve, and that this could be relieved by decompression of the carpal tunnel:

Their cases all had impairment of sensation over the territory of the median nerve, together with wasting of the thenar eminence, and in 1958 Gilliatt and Sears demonstrated delay in nerve conduction at the wrist in such cases. In 1949 McArdle suggested that the common case of acroparæsthesiæ might be the result of a similar mechanism, and this was put to the test by Kremer et al. (1953). They found that division of the flexor retinaculum relieved painful paræsthesiæ which had been referred diffusely to all five fingers, and pain which had been referred diffusely along the ulnar as well as the radial aspect of the forearm, ascending as high as the tip of the shoulder. Neither wasting of thenar muscles, nor impairment of sensation in the median distribution in the hand were necessary signs. They emphasised the predominance of females (especially busy housewives) over males, the paroxysmal worsening of symptoms at night, and the feeling of stiffness and swelling of the fingers in the morning.

This clinical description of the "carpal-tunnel syndrome", was in almost all respects similar to that previously reported by Walshe in lesions of the thoracic and axillary inlets, to many reported examples of cervical-rib compression, and to cervical spondylosis. Various therapeutic measures other than operation were then put forward:

Whereas Roaf (1947) suggested splinting of the wrist, Kendall (1950) recommended a palmar pad; and, in pregnant women, Jones (1953) found salt and fluid restriction successful, while Phalen and Kendrick (1957) gave hydrocortisone injections into the carpal tunnel. The association of acroparæsthesiæ with pregnancy, the menopause, and acromagely, led Young (1950) to postulate an endocrine cause, and he and Reid (1956) showed that œstrogens could induce a remission. Lees and Liversedge (1959) obtained comparable results with prednisone by mouth. But Garland (1957) regarded surgery as the optimum treatment, and some still think it is essential whenever there are objective motor or sensory signs in the territory of the median nerve (Boulter 1959). Crow (1960) has compared the relative efficacy of splinting and hydrocortisone injection; he concludes that hydrocortisone is more reliable than splinting for short-term effect, but that operation gives more certain and lasting results than either. Others, impressed with the association of acroparæsthesiæ and excessive use of the arms, have suggested that accumulation of metabolites within the overworked muscles produces the symptoms (Ford 1956—the "tired arm syndrome"). Others, noting the response of some cases to vasodilators, and the early aggravation when the arm is made ischæmic, have postulated a purely vascular lesion. Thus Pritchard (1950) regarded acroparæsthesiæ as an "organic neurosis due to prolonged spasm of the arterial supply to the nerve", explaining the nocturnal worsening of pain by the release of spasm during sleep.

Russell (1956, 1957, 1958) thinks it is not enough to look on the various varieties of brachial neuropathy as simply due to compression of nerves. The clinical features, such as local tenderness, indicate changes in the interstitial tissue of the nerves which may spread freely from one part to another, with the result that pathological changes in the nerve-roots may, for example, influence vulnerability of the nerves at the wrist. An important consequence of such changes in the nerve-sheaths is that, because the nerves become relatively inelastic, they are vulnerable to the stretching movements inherent in the normal use of the limb. Thus the median nerve at the wrist is stretched by the dorsiflexion associated with gripping; and in fact some patients with the carpal-tunnel syndrome dorsiflex the wrist to

an unusual angle. Operative division of the carpal tunnel may therefore have several effects: it relieves pressure on the nerve; it provides a period of rest after operation; and the operation scar is likely to reduce permanently the angle of wrist dorsiflexion on gripping.

## The Present Study

The brachial neuropathies have long been of special interest to the Oxford neurological department, and we have seen over 800 cases during the past fifteen years. Our policy has always been to study the symptoms and physical signs without any particular attempt to label the condition as a syndrome, and our approach to treatment has been conservative. It was therefore enlightening to analyse a consecutive group of cases seen recently, and to assess the course of the disease by follow-up study. The cases included were all those (total 155) which, during 1955–59 inclusive, presented with symptoms of brachial neuropathy which they had had for more than a month. We excluded any cases due to trauma or carcinomatous deposits, and those with gross paralysis of muscles, as in the syndrome of shoulder-girdle neuritis. 3 cases were excluded in which the information available was inadequate.

There remained 146 cases for analysis. Among these we attempted to follow-up all the 90 patients seen in the three years 1957–59, and where possible to recall them for examination. 82 were traced, and 13 of the earlier patients were also seen because they had to attend hospital for some other reason; this gives a total of 95 cases followed for over a year.

### *Symptoms*

The *duration* of symptoms when first seen was: one to three months in 44 cases; four to six months in 38; seven to twelve months in 17; one to two years in 18; and over two years in 29 cases. The age and sex distribution are given in table I.

*Pain*, which was present in 140 cases, was referred most often to the forearm but it extended to other sites, as shown in table II. It was often diffuse and poorly localised, being sharp, burning, or aching in quality. 99 patients had noticed that the pain or associated tingling was worst in bed at night, 43 found it was maximal on waking, and 74 observed that it was worse after using the limb (this was often a surprisingly delayed effect, the worsening being sometimes six to twelve hours after exertion).

*Numbness* in the hands, especially on rising, was prominent in 67 cases (46%), and unpleasant tingling or burning paræsthesiæ in 103 (70%), the two often occurring together. Such sensations were associated with pain at any level, but this was most often in the forearm, with diminishing frequency towards the neck and scapula. As shown in table II, the site of pain is not influenced by the presence or absence of numbness or paræsthesiæ in the fingers.

Symptoms were *bilateral* in 52 cases; these had a similar distribution of pain but rather more peripheral paræsthesiæ than the group as a whole (86% compared with 70%). The pain clearly radiated downwards in 34 cases, and these had more pain both proximally and distally in the limb.

### *Physical Signs*

We often found *widespread tenderness*, especially over the long flexors of the forearm when this was the seat of maximal pain. Strong development of arm muscles with tenseness of the forearm tendons was very common. 28 patients showed tenderness of the muscles supporting the scapula, and 14 more were tender over the spinous processes of the lower cervical vertebræ. Objective sensory loss—usually hypoalgesia to pinprick—was present in 65, being confined to the territory of the median nerve below the wrist in 45, and taking up a root distribution over the arm or ulnar side of the hand in 20. On percussing over the median nerve at the wrist, paræsthesiæ were produced in the first three fingers in 24 cases.

38 cases had *wasting* of the thenar eminence, 3 of the triceps muscle, and 3 of the interossei and lumbricals. In 21 cases, thenar wasting coincided with sensory loss of median distribution below the wrist. 19 cases showed diminution or absence of one or more tendon reflexes in the affected arm. The symptoms in 17 patients were reproduced or aggravated by movements of the neck (10 had noticed this themselves), and in 12 more the neck movements were restricted in one direction or another. In 7 shoulder movements were restricted by pain, and in 6 the symptoms were definitely aggravated by bracing the shoulders or pulling on the outstretched arm.

Radiographs of the cervical spine, taken in 92 cases, revealed generalised spondylotic changes in 46, and localised loss of disc space in 12 more. 5 patients were found to have cervical ribs, and on myelography 3 were shown to have prolapsed disc tissue.

TABLE I—AGE AND SEX DISTRIBUTION OF THE 146 CASES STUDIED

| Age (yr.) | Male | Female | Total |
|---|---|---|---|
| 20 | 0 | 1 | 1 |
| 21–30 | 2 | 14 | 16 |
| 31–40 | 5 | 25 | 30 |
| 41–50 | 11 | 39 | 50 |
| 51–60 | 9 | 32 | 41 |
| 60 | 3 | 5 | 8 |
| Total | 30 | 116 | 146 |

TABLE II—THE SITES OF PAIN IN ALL CASES, AND IN THOSE WITH PARÆSTHESIÆ AND NUMBNESS IN THE FINGERS

| Site of pain | All 146 cases (%) | 103 cases with paræsthesiæ in fingers (%) | 67 cases with numbness in fingers (%) |
|---|---|---|---|
| Scapula | 8 | 7 | 8 |
| Neck | 29 | 24 | 33 |
| Shoulder | 40 | 35 | 39 |
| Upper arm | 49 | 43 | 43 |
| Forearm | 77 | 75 | 76 |
| Hand | 52 | 51 | 55 |
| Fingers | 49 | 51 | 52 |

### *Treatment*

The methods we used were based largely on the view that vigorous use of the limb is usually the chief factor in maintaining the condition and preventing recovery. Whatever else is done, the limb must be rested.

In many cases rest alone was advised in the first instance. The patient was also told what forms of manual activity were particularly liable to aggravate the condition. This was usually easily decided from the patient's own evidence: in housewives (who formed a large proportion of cases) it consisted of scrubbing, polishing, wringing, knitting, and carrying shopping baskets—i.e., anything involving sustained muscular contraction, especially of the grip.

A sling was often fitted in such a way that the weight of the affected arm was carried on the opposite shoulder; it is important that there should be no pressure on the neck or shoulder on the same side as the pain. When there was clear evidence of median-nerve involvement at the wrist, a plaster-of-paris or plastic splint was sometimes fitted to immobilise the wrist in a neutral position while leaving the fingers free, and this was worn during the day for two to four weeks. Injections of hydrocortisone into the carpal tunnel were given to a few patients, and operative decompression of the carpal ligament was advised for a few particularly severe cases.

When the pain was clearly radicular, or accompanied by signs of nerve-root damage, a small sorbo-rubber collar was sometimes worn for several weeks to restrict gross neck movements, but stricter immobilisation was found to be unnecessary. If there was much tenderness around the scapula, local infiltrations of procaine were often given. Neck traction was occasionally used, sometimes at home with a portable traction set. This, along with shoulder-raising exercises and short-wave diathermy, had sometimes been tried unsuccessfully before the

TABLE III—METHODS OF TREATMENT AND RESULTS

| Method of treatment | Early (3–6 wks.) results in 130 cases* | | | | Late (1–3 yr.) results in 95 cases† | | | |
|---|---|---|---|---|---|---|---|---|
| | Total | Failed | Improved | Cured | Total followed up | Relapsed | Relieved | Symptom-free |
| Rest alone | 31 | 3 | 12 | 16 | 20 | 1 | 7 (3)‡ | 12 (4)* |
| Sling | 59 | 8 | 21 | 30 | 27 | 7 | 4 (3) | 16 (2) |
| Splint to wrist | 18 | 3 | 4 | 11 | 6 | 1 | 0 | 5 (2) |
| Hydrocortisone under carpal ligament | 10 | 1 | 3 | 6 | 4 | 1 | 1 | 2 |
| Operative decompression of carpal ligament | 9 | 1 | .. | 8 | 6 | 0 | 0 | 6 (3) |
| Collar | 22 | 7 | 3 | 12 | 13 | 1 | 1 | 11 (1) |
| Collar + sling | 5 | 0 | 4 | 1 | 3 | 0 | 2 | 1 |
| Procaine to scapular muscles | 10 | 0 | 3 | 7 | 6 | 1 | 1 | 4 (2) |
| Procaine + collar | 4 | 0 | 2 | 2 | 3 | 1 | 0 | 2 (2) |
| Procaine + sling | 5 | 0 | 1 | 4 | 4 | 0 | 1 | 3 (1) |
| Traction to neck | 11 | 7 | 2 | 2 | 1 | 1 | 0 | 0 |
| Freeing of frozen shoulder | 3 | 0 | 0 | 3 | 2 | 0 | 0 | 2 |
| Totals | 187 | 30 | 55 | 102 | 95 | 14 | 17 | 64 |

* When more than one method was used in a case each is entered.
† Assessed for the method ultimately most successful.
‡ Figures in parentheses indicate the number of cases with symptoms for more than a year when first seen.

case was referred to the neurology clinic. Active forms of physiotherapy (massage, heat, &c.) were avoided, and nothing was allowed which interfered with the basic need for rest.

If one method failed, another was tried; a few cases were admitted to hospital, sometimes because rest was impossible at home. The method used initially depended partly on the overall clinical picture and partly on the whim of the particular consultant concerned. We have no means of knowing whether the results would have been different in the individual case with another method.

*Results of Treatment*

Information regarding the early effects of treatment (three to six weeks after first being seen) were available in 130 of the 146 cases. 94 had ultimately been completely relieved of all symptoms, and the others (36) had all been improved, often to such a degree that no further treatment seemed necessary.

Table III indicates the varieties of treatment used, and their respective success. In many of the 130 cases more than one method was used (in succession), giving a total of 187 methods of treatment in 130 cases.

*Late follow-up.*—95 cases were seen after more than a year (22 at twelve to eighteen months, 22 at eighteen to twenty-four months, 38 at two to three years, and 13 at more than three years). 64 were found to be free of all symptoms, 17 were relieved, and 14 had neuritis as much as before (table III). Among those cured were 17 who had had symptoms for over a year when first seen. In general, the cases which had relapsed at the late follow-up were those which responded inadequately to treatment in the early weeks.

It therefore emerges that the great majority of our cases of brachial neuropathy were completely relieved by conservative measures, even though there had been a long history of pain before treatment.

## Analysis of the Present Series

We tried to correlate the site of the chief symptoms and signs, whether peripheral or proximal, with the type of treatment which was most effective. Few clear correlations could be found, however, for patients with a carpal-tunnel syndrome were often relieved by a sling or a light collar, whereas some with pain in the proximal arm were relieved by splinting the wrist.

In particular 3 patients whose symptoms were reproduced by neck movements, and 2 whose symptoms had been aggravated by depression of the shoulders, were eventually cured by treatment at the wrist. Also 2 patients clearly showing Tinel's sign at the wrist obtained complete relief from neck traction and procaine injections into the scapular muscles respectively.

The time relationships of the pain—worse at night, on waking, or after use (Cyriax 1959, *Post Graduate Medical Journal* 1959)—were found to be of little significance in deciding the level of origin. But aggravation by coughing and straining seems to be a good indication of irritation high in the plexus.

While such signs and symptoms are certainly valuable in indicating where treatment should first be directed, it seems that the process is sometimes diffuse, with widespread sensitivity at several levels along the course of the nerve. Hence the value of applying conservative measures at more than one level, or of resting the entire arm in a sling before proceeding to a more radical attack at the carpal tunnel, intervertebral foramen, or elsewhere.

To assess the relative frequencies of the groups commonly described, we attempted to subdivide our cases. This was largely done retrospectively, and the figures can be approximate only.

78 cases could be regarded as carpal-tunnel syndromes, 50 as irritation of the cervical roots, and 3 as compression at the thoracic outlet; 3 responded promptly to mobilisation for a "frozen shoulder". The other 12 had widespread diffuse pain without any abnormal signs, and this was cured by rest in a sling, and could not therefore be ascribed to any group.

### CARPAL-TUNNEL SYNDROME

These 78 cases had most symptoms in the territory of the median nerve below the wrist, but they often had pain radiating far up the arm. They included most of the patients with objective signs of median-nerve damage; 34 showed wasting of thenar muscles, 29 showed sensory loss in the median territory, and 20 showed both together. 21 cases had a positive Tinel's sign at the wrist. The cervical spine was X-rayed in 34 cases, and spondylotic changes were present in 19.

The response to treatment, for the 47 cases followed up, is shown in abbreviated form in table IV. Many obtained permanent benefit without recourse to operation. Some writers have maintained that operative decompression of the carpal tunnel is always indicated once motor or sensory deficits are established within the territory of the median nerve (Brain 1947, Boulter 1959). It is, therefore,

TABLE IV—RESULTS OF TREATMENT USED IN 47 CASES OF CARPAL-TUNNEL SYNDROME

| Method applied | No. followed up | No. remaining cured* |
|---|---|---|
| Rest | 15 | 9 |
| Sling | 16 | 10 |
| Splint | 6 | 5 |
| Hydrocortisone | 4 | 2 |
| Operation | 6 | 6 |
| Total | 47 | 32 |

* Follow-up was for over one year.

important that of 18 cases with thenar wasting who were treated conservatively, 12 had remained cured when seen at late follow-up. Similarly, of 17 with objective sensory loss 12 remained cured, and of 10 with both wasting and sensory loss 7 responded permanently. In the majority, all abnormal signs had disappeared. For example:

A 54-year-old lorry driver, had for three months experienced severe pain spreading from the wrist to the elbow of the right arm, with tingling of the fingers, worse after driving and at night. There was weakness and wasting of the thenar eminence, and hypoalgesia to pinprick over the tips of the first three fingers. The wrist was immobilised in plaster-of-paris for a week, and then an anterior splint was applied by day for two more weeks. All symptoms disappeared within a few days, and when he was seen two years later they had not recurred. The thenar muscles were normal, and there was no impairment of any modality of sensation.

### ROOT SYNDROMES

In 50 cases the nerve-roots seemed to be involved. The pain was usually sharp and often sudden in onset, and it often spread down the arm from the neck or scapular region. In 42% the pain reached the fingers themselves, and in 60% it was accompanied by paræsthesiæ in the fingers. These included the majority of cases with radicular sensory impairment or muscle wasting other than of the thenar eminence, and all the symptoms were aggravated by coughing and straining. Localised muscle wasting or weakness was present in 6 cases—3 in the triceps, and 3 in the small hand muscles. Abnormality of tendon reflexes was noted in 15, and sensory loss of radicular distribution in 15. There was focal tenderness in the muscles supporting the scapula in 21 cases, and over the spines of the cervical vertebræ in 13. The cervical spine was X-rayed in 42 cases, showing spondylotic changes in 16, and localised loss of disc space in 11; the narrowing of the disc space coincided with clinical localising signs in 7 cases. In 3 prolapsed disc tissue was demonstrated by myelography.

The response to treatment was in general good, and of 37 patients followed for over a year, 29 were relieved of all symptoms. In no case was there any operative intervention on the cervical spine.

The value of injecting procaine into tender spots in the trapezius and medial scapular muscles is often remarkable. 5 patients who failed to show any improvement after immobilisation of the neck for long periods (2 had previously had the neck completely immobilised in plaster-of-paris for many weeks) obtained complete relief from procaine injections. 4 had remained symptom-free when seen two to three years later; 2 had shown localised loss of disc space on cervical X-ray, and the other two had prolapsed disc tissue on myelography. The following case-histories are illustrative:

A man of 35 [78839] had had a constant severe ache spreading from the scapula down the lateral side of the right arm, with tingling in the first three fingers for fourteen weeks, which prevented him from going to work. The condition was aggravated by using the arm or by any movement at the shoulder. His neck movements were painful and restricted in all directions, but his shoulder movements were free. Muscle power and tendon reflexes were normal, but sensation was blunted over the tips of the index and middle fingers. The muscles medial to the right scapula and of the forearm were very tender, and percussion over the median nerve at the wrist produced tingling in the first three fingers. Deep palpation over the tender scapular muscles reproduced the ache in the arm and the tingling in the fingers. X-ray of the cervical spine was normal. He had previously been treated for two months by immobilisation of the head and neck in plaster-of-paris, without effect. However, a single injection of procaine into the tender scapular muscles abolished his symptoms immediately, and he was then fitted with a sling to rest the arm completely. After two weeks' sling rest, during which he remained symptom-free, he returned to work. He had remained cured when seen six weeks later.

A woman of 47 [13011] had for four years had pain between the shoulder blades and radiating down the left arm, aggravated by extending the neck or any sudden jar to the body. She was free from pain only when lying still on her back, or during neck traction. Muscle power, tendon reflexes, and sensation were normal. There was extensive tenderness over the lower cervical spine, scapular muscles, and first and second right intercostal spaces. Myelography showed a bar-shaped filling defect at C6–7, which was presumed to be due to a prolapsed intervertebral disc. Previous treatment, which had included a collar, and complete immobilisation of the neck in plaster-of-paris for four months, had given only partial and temporary relief of symptoms. Before considering operative exploration of the disc, lignocaine was injected at the points of maximal tenderness over the cervical spine and around the scapula, and this produced dramatic relief of symptoms. Three months later she was still greatly improved, and further injections were given. Two years later, she had had no further severe pain, but had occasional discomfort between the shoulder blades in relation to sudden movements when doing housework, and preferred to wear a sorbo collar at such times. She dated the relief of her symptoms from the first injection.

It can only be presumed that procaine acts by temporarily diminishing the afferent flow into an irritable focus within the spinal cord, and thereby interrupting a vicious circle. Procaine does not seem to affect cases which differ in any way from those in which immobilisation of the neck is successful.

### THORACIC-OUTLET SYNDROMES

It is more difficult to gauge the frequency with which irritation at the thoracic outlet is the major cause of the neuropathy. 41 cases were treated with a sling disposed to raise the shoulder on the affected side, but the majority of these were easily included in one or other of the preceeding groups, and only 3 showed symptoms mainly in the distribution of the lower components of the brachial plexus. In 2 of these X-rays showed cervical ribs; the other patient was persistently tender over the insertion of scalenus anticus, and percussion there reproduced the typical pain and paræsthesiæ in the arm and fingers.

Altogether, cervical ribs were found in 5 of the 92 cases in which the cervical spine or thoracic inlet was X-rayed, and 6 cases were tender over the insertion of scalenus anticus; but, apart from the cases mentioned above, all closely resembled the cases included in the two preceding groups. Similarly, in 6 cases the radial pulse could be reduced by bracing the shoulders or pulling on the arm; but except for 1 (included above) there was evidence suggestive of a lesion elsewhere in the brachial nerves. Indeed, the high proportion of cases in which such manœuvres affect the pulse in normal adults has been reported by Stammers (1950). We think, therefore, that very few of our cases of brachial neuropathy originate from the region of the thoracic outlet, though this may often be an important contributory factor, and that the recognition of nerve-root and carpal-tunnel compression has reduced the importance of the many mechanisms once described in this region.

### DIFFUSE NEUROPATHIES AFFECTING SEVERAL LEVELS

In many instances the painful neuropathy had spread to involve all levels of the brachial nerves by the time the

patient was first seen. Sometimes the symptoms could be aggravated equally by palpating the brachial plexus in the supraclavicular fossa or by tapping the median nerve at the wrist. In longstanding neglected cases, such generalised sensitivity at all levels of the brachial plexus can sometimes be striking:

A woman of 36 had severe aching which spread from the scapula, across the shoulders, down both forearms, and into all the fingers of both hands. This had been present for three years, with tingling of the fingers at night and numbness on waking in the morning. Despite aggravation on using the arms, she had continued to do extra work, and when finally seen she had widespread tenderness around the shoulder-girdle muscles, in the supraclavicular fossæ, and over the anterior forearm muscles. Tapping over the insertion of scalenus anticus reproduced sharp pain down the whole arm and into the fingers, and percussion over the median nerve at the wrist produced paræsthesiæ in the hand and first three fingers. Sensation to pinprick was diminished over the lateral half of both palms, but there was no thenar wasting. The condition resisted several forms of treatment, but it finally responded to a week's rest in bed with periods of neck traction.

## Discussion

In tracing the history of brachial neuropathy it is clear that lesions situated at widely different points along the course of the nerves have been blamed for one and the same syndrome. Time and again the demonstration of a new and convincing mechanism in a small group of cases has been followed up with enthusiasm, and treatment based on the new theory has often given enough cures to uphold that theory for a long time.

A possible reason is that, in many cases, multiple factors operate together at more than one level along the course of the nerves (Russell 1956, 1958). Certainly there is a free intraneural circulation between the nerve-roots and the peripheral parts of the nerve (Brierley and Field 1949); and it seems probable that pathological changes at one level, say the nerve-root, may influence the vulnerability at others. In fact, in severe cases, local tenderness can sometimes be demonstrated along the entire length of the involved nerves, and such diffuse involvement would also explain the extensive area over which pain is commonly referred. As already mentioned, vulnerability to stretching probably influences the clinical picture a good deal.

Study of our cases supports this hypothesis by showing the considerable clinical similarity in cases responding to treatment directed at different levels, and by showing, in many cases, signs of nerve damage or sensitivity at different levels. This is not to suggest that " pure " examples of nerve-root, thoracic-inlet, or carpal-tunnel compression do exist. There is very strong evidence that they do; but in our cases there seemed to be much overlap. It is important to realise how far the clinical signs may be misleading, and to remember that response to treatment at one particular level does not necessarily mean that the pathological process was confined to, or even maximal at, this level. Kibler and Nathan (1960) have clearly shown, for example, that both pain and paræsthesiæ can be abolished by anæsthetising a nerve distal to the lesion which caused them. It may therefore be unjustifiable to assume that, when brachial neuropathy is relieved by, say, dividing the carpal ligament at the wrist, factors proximal to this were not helping to maintain the original condition.

This, of course, has an important bearing on treatment in that attention should not always be focused exclusively on the part of the process which is obvious to clinical examination. This is especially true in the difficult or " resistant " case, which may respond strikingly when all levels of possible irritation to the nerves are borne in mind and treated. This can be done most effectively by a period of enforced rest for the whole limb—for example, by applying a sling in the way described. Operation on the carpal tunnel or intervertebral foramen, or removal of an abnormality at the thoracic outlet, can always be kept in reserve while simpler outpatient procedures are tried in rotation or combination. In this way the expectation of success is high. The results in our series suggest that, when the optimum method of treatment has been found, its effect may be expected to persist. It is also evident that long-continued symptoms, or physical signs which indicate impaired nerve function, need not dictate more radical treatment at the outset.

We would draw attention to the relative infrequency with which operation on the carpal tunnel was required in our patients, and to the absence of need for operation on the nerve-roots or thoracic inlet. Indeed we are doubtful whether the present enthusiasm for operating either on the carpal tunnel in Britain, or on the cervical nerve-roots in the United States, will last. The results of conservative treatment are so good that they require careful assessment in relation to the effects reported after operation. Finally we hope that this study will form a background against which other methods of treatment can be compared.

## Summary

The theories of ætiology of brachial neuropathy, and the methods of treatment available, are outlined.

The clinical signs and symptoms in a consecutive series of 146 cases seen in a neurological clinic are analysed, and the methods of treatment are assessed both for immediate effect and on follow-up of 95 cases one to three years after treatment.

Conservative methods of treatment were valuable, and the results compare favourably with those of other reported series treated surgically.

There is much overlap between conventional clinical syndromes, and evidence is presented that in many cases there is diffuse involvement of nerves along their entire course.

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# HÆMOPHILIA SYNDROMES

## A Survey of 267 Patients

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THE older surveys of hæmophilia, best exemplified by those of Bullock and Fildes (1912) and of Birch (1937) were mainly concerned with establishing the clinical features of the disease and the mode of its inheritance. Surveys published during the last twelve years have been more informative because new techniques have enabled us to detect the characteristic blood-clotting defect even though less than two-thirds of the patients may show a prolonged clotting-time.

In 1949 Quick and Favre-Gilly described their prothrombin-consumption test which, often used in the modified form proposed by Merskey (1950), made it possible for about 85% of the cases to be identified. In 1953 Biggs and Douglas published details of their thromboplastin-generation test with which practically all hæmophilic cases can be detected; this test also paved the way for the identification of Christmas disease and the other rarer syndromes which, although clinically indistinguishable from classical hæmophilia, are in fact due to deficiencies of other factors. In 1957 Biggs proposed a method, based on the thromboplastin-generation test, for estimating the actual deficiency of the antihæmophilic globulin.

With the help of these techniques more recent surveys have included clinically mild cases that had previously escaped detection. All the new information has strengthened the idea that hæmophilia is inherited as a sex-linked recessive carried on the X chromosome. The only departures from this mode of inheritance so far reported occurred in the family described by Wilkinson et al. (1957) in which a pair of hæmophilic females, properly descended from a hæmophilic father and a carrier mother, produced hæmophilic daughters though their husbands were not affected, and in a family reported from Finland by Ikkala (1960).

Since 1953 a few surveys reporting results with considerable numbers of patients have been published.

den Ottolander (1955) in Holland collected 129 patients (119 hæmophilia and 10 Christmas disease), and calculated that the prevalence was about 1 in 10,000 of the population. He noted that in 28% of the hæmophilic families there was no previous history of the disease. Biggs and Macfarlane (1958) reported 187 cases, including 138 of hæmophilia, 20 of Christmas disease, and 3 of Rosenthal's "P.T.A. deficiency"; they were mainly concerned with finding out how far laboratory tests could be linked with the clinical severity and so used to predict the clinical course. They found that 37·6% of the hæmophilic patients had clotting-times of over 30 minutes and all these patients were severely affected; 37% had normal clotting-times; but though all the mild cases were in this group, some severe cases were also included. Assays of antihæmophilic globulin (A.H.G.) were made in 115 patients; in 63 there was no detectable A.H.G., the other 52 showed various assays up to 49% of normal; all patients with more than 5% A.H.G. were classified as "mild". All their severe cases had less than 2%; in most of them none was detectable in the plasma. But the A.H.G. assay did not enable Biggs and Macfarlane to predict with certainty the likelihood of bleeding after operations such as tooth extraction; in general, patients with less than 10% A.H.G. fared worse than those with more than 10%. Ikkala (1960) was able to divide 116 clinically hæmophilic patients into 87 with classical hæmophilia and 29 with Christmas disease. He gave details of 73 pedigrees, and in one family the inheritance was anomalous: a hæmophilic father and a carrier mother had a carrier daughter; the daughter married a normal male, and, of their three children, one was a normal male, one a hæmophilic male, and one a hæmophilic female with 1·5–2% A.H.G. A.H.G. assays were carried out on 82 patients, 62 had 0–5%; 11 had 5–10%; and 9 had more than 12%. Ikkala considered that in general the clinical severity accorded with the assay, the three groups corresponding to severe, fairly severe, and mild cases. He pointed out the long life expectancy of all except the mildest cases. The latest survey is that reported from Denmark by Sjølin (1961), who has details of 148 patients, about 1 in 27,000 of the population. His group, which is remarkable for the number of patients with unusual syndromes or with deficiencies of more than one factor, included 72 patients with hæmophilia, 33 with Christmas disease, 3 with P.T.A. deficiency, and 11 with Hageman-factor deficiency; 25 were said to have combined A.H.G. and Christmas-factor deficiency. Sjølin noted that in his hæmophilic group bleeding occurred in the first year of life in about 70%, 92% had hæmarthroses, and 59% had permanent joint deformities; a third of the group were normally fit for work, a third were unfit for manual work, and a third were "partially fit". A third of the Christmas-disease patients were disabled, but 2 had carried out their military service.

The group report here includes all the patients we have had under our care in the twenty-five years from Jan. 1, 1936, to Dec. 31, 1960; some patients who have been seen by us in Manchester but who are normally under the care of other centres have not been included. We have set out the distribution of clinical features and attempted to assess the burden of the care of such a group; we have classified the results of laboratory tests and endeavoured to relate some of them to the clinical severity.

### Techniques

We have used standard techniques throughout. For whole-blood clotting-time the method of Lee and White has been used; the prothrombin-consumption index has been estimated by the method of Merskey (1950); for A.H.G. assay we have used the technique of Biggs (1957). The Bridge anticoagulant effect has been estimated by the technique of Nour-Eldin and Wilkinson (1958).

### Results

The results are presented in the accompanying tables.

In the period under survey (Jan. 1, 1936, to Dec. 31, 1960, we have seen 267 patients; 229 of these had classical hæmophilia (hæmophilia A), 38 (15·9%) had Christmas disease (hæmophilia B); this proportion of 15·9% for Christmas disease is of the same order as that found by

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TABLE I—AGE-GROUPS IN 267 PATIENTS WITH HÆMOPHILIA SYNDROMES (229 HÆMOPHILIA, 38 CHRISTMAS DISEASE)

| Age-group (yr.) | Hæmophilia | | Christmas disease | |
|---|---|---|---|---|
| | First detected | First seen in dept. | First detected | First seen in dept. |
| 0–5 | 196 | 68 | 35 | 12 |
| 6–10 | 13 | 28 | 2 | 7 |
| 11–20 | 10 | 51 | 1 | 4 |
| 21–40 | 10 | 54 | 0 | 10 |
| Over 40 | 0 | 28 | 0 | 5 |

other European workers except Ikkala (1960) in Finland who reported 33%. Five of our hæmophilic patients were females, and 4 of these were in one family (Israëls et al. 1951, Wilkinson et al. 1957). A positive family history was obtained in 182 patients (60%). During the review period we did not find any cases of Rosenthal's P.T.A. deficiency or of the Hageman-factor deficiency.

Table I shows the distribution of the ages when the disease was first diagnosed and the ages when the patients were first seen by us. It will be noticed that most cases had been diagnosed by the time the patient was 5 years old, only 13% being diagnosed later than this age. No less than 97 patients were over the age of 20, including 33 over the age of 40, when they first came to the department for advice. A few of them had been under the care of other hospitals, quite a lot came because dental extractions had become necessary, and others came because they realised that something could be done for them.

TABLE II—CAUSES OF DEATH IN HÆMOPHILIA SYNDROMES

| Cause of death | Age of patient (yr.) | No. |
|---|---|---|
| Alimentary-tract bleeding | 11, 13, 24, 24, 59 | 5 |
| Cerebral hæmorrhage | 9, 26, 58, 60, 63 | 5 |
| Retroperitoneal hæmorrhage (not operated on) | 8, 29 | 2 |
| Retroperitoneal hæmorrhage (operated on) | 23, 24 | 2 |
| Motor accidents | 20, 23 | 2 |
| Intestinal obstruction (operated on) | 31 | 1 |
| Carcinoma of cæcum (operated on) | 45 | 1 |
| Subdural hæmatoma | 69 | 1 |
| Bronchopneumonia | 78* | 1 |
| Total | | 20 |

* Christmas disease.

In our series 20 have died; and it will be seen (table II) that hæmophilia is surprisingly not a killing disease, at least when proper facilities for the treatment of hæmorrhage are available. The most dangerous symptoms are clearly alimentary-tract bleeding and cerebral hæmorrhage; 13 of our patients had signs of cerebral hæmorrhage, which proved fatal in only 5 of them. The deaths following surgical operations occurred in the earlier part of the observation period; the chance of recovery for these patients is much better today with present methods of handling emergencies.

TABLE III—FIRST SIGNS IN HÆMOPHILIA SYNDROMES (227 HÆMOPHILIA, 38 CHRISTMAS DISEASE)

| Cause of bleeding | Hæmophilia | Christmas disease | Total |
|---|---|---|---|
| Excessive traumatic bleeding | 55 | 10 | 65 |
| Spontaneous bruising | 55 | 7 | 62 |
| Hæmarthrosis | 41 | 5 | 46 |
| Bleeding due to dental disease, before or after tooth extraction | 40 | 4 | 44 |
| Epistaxis | 14 | 4 | 18 |
| Circumcision | 9 | 7 | 16 |
| Tonsillar bleeding | 4 | 0 | 4 |
| Hæmaturia | 1 | 1 | 2 |
| Alimentary-tract bleeding | 2 | 0 | 2 |
| Central-nervous system hæmorrhage | 1 | 0 | 1 |
| Throat and sublingual hæmorrhage | 2 | 0 | 2 |
| Pyloric-stenosis operation at 6 mos. | 1 | 0 | 1 |
| Vaginal bleeding after labour | 1 | 0 | 1 |
| Ectopic bladder | 1 | 0 | 1 |

The first signs that drew attention to the patient's condition are summarised in table III, where these are arranged in order of frequency. The commonest first signs are the relatively mild ones, and in 48% were due to either excessive traumatic bleeding or spontaneous bruising. Hæmarthrosis (47·5%) is well known to be a relatively common first sign. The child with an ectopic bladder was successfully treated surgically; the patient whose postpartum hæmorrhage drew attention to her disease is the woman already reported (Israëls et al. 1951). The 16 circumcisions were all carried out in infancy and this is one of the first and the longest-known signs.

TABLE IV—HÆMORRHAGIC SYMPTOMS IN HÆMOPHILIA SYNDROMES (HÆMOPHILIA AND CHRISTMAS DISEASE COMBINED, 267 CASES)

| Symptom | Patients affected | |
|---|---|---|
| | No. | % |
| Traumatic bleeding, excessive | 246 | 93·0 |
| Hæmarthrosis | 177 | 66·4 |
| Spontaneous bruises and hæmatoma | 174 | 65·2 |
| Bleeding from gums | 167 | 62·5 |
| Epistaxis | 101 | 38·8 |
| Hæmaturia | 63 | 23·6 |
| Alimentary-tract bleeding | 51 | 19·0 |
| Retroperitoneal hæmorrhage | 33 | 12·3 |
| Throat and sublingual hæmorrhage | 33 | 12·3 |
| Circumcision | 21 | 7·8 |
| Central-nervous-system hæmorrhage | 13 | 4·8 |
| Peripheral-nerve hæmorrhage | 12 | 4·5 |
| Tonsillar hæmorrhage | 11 | 4·2 |
| Hæmothorax | 4 | 1·5 |
| Purpura | 2 | 0·8 |
| Others | 9 | .. |

The important symptoms (table IV) in the hæmophilia syndromes are listed in order of their frequency; and it will be seen that excessive bleeding after trauma, hæmarthrosis, spontaneous bruising and occurrence of hæmatomata often in muscles, and bleeding connected with dental conditions are the commonest symptoms by a large margin. Others are considerably less frequent; and this is fortunate since, with the possible exception of epistaxis, they are all more difficult to manage than the four most frequent symptoms. Table IV brings out the relative rarity of hæmorrhage into the central nervous system, and this again is fortunate since it is one of the most dangerous manifestations; 5 of the 13 patients so affected died (see table II).

TABLE V—DENTAL DISEASE IN HÆMOPHILIA SYNDROMES (229 PATIENTS WITH HÆMOPHILIA, 38 PATIENTS WITH CHRISTMAS DISEASE)

| — | Hæmophilia | | Christmas disease | | Total | |
|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % |
| Patients needing dental treatment | 138 | 60·2 | 24 | 62·0 | 162 | 60·7 |
| Patients needing transfusion for dental treatment | 105 | 45·8 | 18 | 47·5 | 123 | 46·0 |

Dental treatment has been required in 162 (60·7%) of our patients (table V), and no less than 40% of them in the course of their dental treatment have needed blood-transfusion control which has meant admission to hospital for seven to ten days. Patients with hæmophilia and with Christmas disease show very similar figures (table V). Considerable amounts of blood or plasma have been used (table VI) to enable these patients to be treated successfully. Fortunately, urgent dental extraction is not often called for and our policy has been to put such

TABLE VI—BLOOD USED IN TREATING HÆMORRHAGIC COMPLICATIONS IN HÆMOPHILIA SYNDROMES *

| Cause of bleeding | No. of incidents | Total amount of blood (pints)† | Average blood per incident (pints) | Max. blood for any one incident (pints) |
|---|---|---|---|---|
| Teeth | 122 | 545 | 4·5 | 18 |
| Trauma | 80 | 149 | 1·8 | 11 |
| Alimentary tract | 67 | 577 | 8·6 | 70 |
| Hæmarthrosis | 50 | 77 | 1·5 | 4 |
| Epistaxis | 57 | 182 | 3·2 | 35 |
| Hæmaturia | 19 | 62 | 3·2 | 17 |
| Others | 77 | 233 | 2·9 | 37‡ |

* Hæmophilia and Christmas disease combined.
† Plasma is recorded as the amount of blood used to prepare the plasma.
‡ Hysterectomy in a female hæmophiliac.

patients on the waiting-list as soon as our dental surgeon reports that extractions are essential. We have described our technique (McIntyre et al. 1959), and by carrying out multiple extractions we have reduced very considerably the time spent in hospital and the amount of fresh blood required. Even so we usually have a list of about 20 patients awaiting admission for dental treatment.

Dental treatment and the management of alimentary-tract hæmorrhage require the most blood. With dental treatment there were many incidents, but the average amount for each patient is not large and the most needed for one patient was 18 pints. With alimentary-tract hæmorrhage nearly twice as much blood is needed for each incident, and the 70 pints for one incident is the largest amount we have ever needed so far.

TABLE VII—BED OCCUPATION BY HÆMOPHILIC PATIENTS AT MANCHESTER ROYAL INFIRMARY

| Period | Total days spent in hospital | Beds continuously occupied |
|---|---|---|
| 1951–53 | 818 | 0·7 |
| 1954–56 | 2934 | 2·7 |
| 1957–59 | 2548 | 2·3 |
| 1960 | 1024 | 2·8 |

The blood requirements for the treatment of other frequent complications of hæmophilia are shown in table VI. Traumatic hæmorrhage is relatively easily controlled, but most of the incidents are usually minor ones.

The running of a hæmophilia centre involving a group of 267 patients implies in practice a considerable responsibility and a constant and regular need for, and utilisation of, hospital beds for their proper care (see table VII). The bed occupancy for our clinic seems to have settled to a relative stability and probably represents the minimum if reasonable care is to be achieved. We have few beds available for all the cases of blood diseases, and so hæmophilic patients never remain longer in hospital than is absolutely necessary, and are transferred to outpatient treatment whenever possible. Unfortunately there are practical difficulties in arranging fresh-blood transfusions for hæmophilic outpatients, although patients with Christmas disease can often be treated with 5-day-old blood or plasma in this way.

The results of the laboratory tests on our patients are shown in tables VIII-X. The distribution of the ABO blood-groups together with the Rh(D) groups (table VIII) in our hæmophilic patients does not differ significantly from the normal, and the proportion of Rh(D) positive patients is about the expected 80%.

TABLE VIII—BLOOD-GROUP DISTRIBUTION IN HÆMOPHILIA SYNDROMES (266 CASES)

| Group | No. | % | Normal percentage * |
|---|---|---|---|
| Group O, Rh-positive | 94 | .. | .. |
| „ O, Rh-negative | 24 | .. | .. |
| Total group O † | 122 | 45·8 | 46·7 |
| Group A, Rh-positive | 93 | .. | .. |
| „ A, Rh-negative | 15 | .. | .. |
| Total group A ‡ | 111 | 41·8 | 41·7 |
| Group B, Rh-positive | 19 | .. | .. |
| „ B, Rh-negative | 6 | .. | .. |
| Total group B | 25 | 9·3 | 8·6 |
| Group AB, Rh-positive | 7 | .. | .. |
| „ AB, Rh-negative | 1 | .. | .. |
| Total group AB | 8 | 3·1 | 3·0 |

* From Dobson and Ikin (1946) quoted by Race and Sanger (1958).
† Includes 4 patients whose Rh group was not known.
‡ „ 3 „ „ „ „ „ „ „

The results of the three common tests of blood-clotting in table IX reflect the increased efficiency of detection; normal clotting-times were found in 41·7% of the hæmophilic patients, and 52·6% of those with Christmas disease; the figures for normal prothrombin-consumption were 10·6% and 17·4% respectively, whereas we have so far not found a single patient with a normal thromboplastin-generation test who can be firmly diagnosed as having either of these syndromes. We have not yet encountered a patient with both antihæmophilic-globulin deficiency and Christmas-factor deficiency.

TABLE IX—RESULTS OF LABORATORY TESTS IN HÆMOPHILIA SYNDROMES

| Test | Hæmophilia | | Christmas disease | |
|---|---|---|---|---|
| | No. | % | No. | % |
| *Coagulation-time (Lee and White):* | | | | |
| Normal up to 10 min. | 94 | 41·7 | 20 | 52·6 |
| 11–29 min. | 41 | 18·3 | 10 | 26·4 |
| 30 min. and more | 90 | 40·0 | 8 | 21·0 |
| *Prothrombin-consumption index (Merskey):* | | | | |
| Normal less than 10% | 19 | 10·6 | 6 | 17·4 |
| 10–40% | 49 | 27·6 | 9 | 26·8 |
| Over 40% | 110 | 61·8 | 19 | 55·8 |
| *Thromboplastin-generation test:* | | | | |
| Normal | 0 | 0·0 | 0 | 0·0 |
| A.H.G. deficiency | 214 | 100·0 | 0 | 0·0 |
| Christmas-factor deficiency | 0 | 0·0 | 38 | 100·0 |

TABLE X—CLINICAL GRADE, A.H.G. ASSAY, AND BRIDGE ANTICOAGULANT

| Clinical grade * | A.H.G. assay | | | | | | | Bridge anticoagulant † | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Total cases in grade | No. of cases with: | | | | | | Total cases in grade | No. of cases with index: | | | | | |
| | | 0 | Up to 1% | Up to 2% | Up to 4% | Up to 8% | Up to 16% | | 1 | Up to 2 | Up to 3 | Up to 4 | Up to 5 | >5 |
| 1 | 4 | 1 | 2 | .. | .. | .. | 1 | 4 | 1 | 3 | .. | .. | .. | .. |
| 2 | 20 | 6 | 2 | 2 | 2 | 3 | 5 | 15 | 1 | 12 | .. | 1 | .. | 1 |
| 3 | 19 | 11 | 2 | .. | 2 | 2 | 2 | 9 | .. | 6 | 1 | 1 | .. | 1 |
| 4 | 22 | 21 | 1 | .. | .. | .. | .. | 20 | .. | 7 | 8 | 2 | .. | 3 |
| 5 | 2 | 2 | .. | .. | .. | .. | .. | 2 | .. | 1 | 1 | .. | .. | .. |
| Totals | 67 | 41 | 7 | 2 | 4 | 5 | 8 | 50 | 2 | 29 | 10 | 4 | .. | 5 |

* See text discussion of table X.
† Thromboplastin generation test after 6 min. incubation:
$\frac{\text{Time with patient's plasma substrate}}{\text{Time with normal plasma substrate}}$ = index. Normally 1.

In table X are shown the figures for A.H.G. assay and for an estimate of Bridge anticoagulant activity; these figures have been related to an assessment of clinical grade. The clinical grades are as follows:

*Grade 1.*—Very mild. No hæmorrhages apart from trauma or tooth extraction.

*Grade 2.*—Mild. As grade 1 plus one other symptom; patient rarely in hospital.

*Grade 3.*—Moderate. As grade 2 with several hæmorrhagic symptoms; occasional hospital admission.

*Grade 4.*—Severe. Multiple hæmorrhagic episodes, frequent hospital admission.

*Grade 5.*—Very severe; unable to work.

The results for antihæmophilic globulin show that 63% of the patients tested had no detectable A.H.G. in their plasma. Only 1 out of the 24 patients in the two "severe" grades had any A.H.G., and this patient's clinical severity was related more to the presence of a duodenal ulcer than to his hæmophilia. The milder grades showed a considerable variation in the levels found. In practical terms this means that the absence of detectable A.H.G. does not necessarily mean that the patient is, or will be, severely affected; he may be quite mildly affected throughout life. On the other hand the presence of an A.H.G. level of only 1% of normal puts the patient into one of the milder grades, though it is possible to have over 8% and still have several symptoms needing occasional hospital admission. These findings are in general agreement with those of Biggs and Macfarlane (1958).

The estimates for the Bridge anticoagulant show that 58% of the patients of all clinical grades had an index between 1 and 2—i.e., that the thromboplastin-generation-test clotting-time using the patient's own plasma as a substrate was up to twice as long as the test clotting-time using standard normal plasma as substrate. But of 19 patients with an index greater than 2, 14 (74%) were in two severe grades (4 or 5). The Bridge anticoagulant results are thus of value in picking out cases likely to be severe; if the index is up to 2, no prediction of clinical grade is possible, but if it is over 2 the case is likely to be severe. The Bridge anticoagulant results are then complementary to the A.H.G. results, which predict particularly the mild cases. It is not really surprising that these tests of blood-clotting fail to provide the basis for a precise clinical assessment; the difficulties with the healing of wounds, for instance, suggest that other systems may be affected by the genetic abnormalities of the hæmophilia syndromes.

The figures given in these tables tend to emphasise the disabilities of the hæmophilia syndromes; the many hazards the patients are exposed to; and the amount of effort, in terms of bed-space, blood-transfusions, and laboratory investigation, that is expended in their care. But, in fact, many hæmophilic patients can lead almost normal lives, special care being needed only for dental treatment. A few figures show this better side of the picture:

Patients aged 15 or over when first seen by us at the Manchester Royal Infirmary numbered 132; 120 (91%) were working at the time or were still at a normal school; only 12 (9%) were without occupation. We have adequate information about remissions in 237 patients; only 87 of them (36·4%) had two years or less between hæmorrhagic episodes; 57 of them (24·0%) had been free from hæmorrhage for more than ten years. The proportions of patients with classical hæmophilia and Christmas disease in this long-remission group—87·7% hæmophilia and 12·3% Christmas disease—are not significantly different from the proportions in the whole group. Christmas disease does not seem to be clinically milder than hæmophilia.

## Summary

A survey of the patients with hæmophilia syndromes seen at Manchester Royal Infirmary between Jan. 1, 1936, and Dec. 31, 1960, is reported. There were 267 patients, of whom 229 (84·1%) had classical hæmophilia and 38 (15·9%) had Christmas disease.

231 patients had been diagnosed by the age of 5 years, but 10 were over 20 years old. The commonest first signs were: excessive traumatic bleeding (65 patients), spontaneous bruising (62 patients), hæmarthrosis (46 patients), and bleeding due to dental complications (44 patients); these, with the addition of epistaxis, were the commonest hæmorrhagic symptoms. Hæmaturia affected 63 patients, and throat and sublingual hæmorrhages 33; central-nervous-system hæmorrhage was found in only 13 patients, and hæmorrhage involving peripheral nerves in 12. Only 20 deaths occurred, alimentary-tract hæmorrhage (5 patients) being the most frequent cause.

So far 123 patients (46%) have needed blood-transfusions to cover dental treatment, and the largest amount of blood (545 pints) has been used in this way. Alimentary-tract hæmorrhage accounted for the largest amount of blood used in any one incident (70 pints).

Between 2·3 and 2·8 beds are continuously occupied throughout the year at Manchester Royal Infirmary by hæmophilic patients.

The blood-group distribution was normal. 114 patients had normal whole-blood clotting-times, and 25 had normal prothrombin consumption; but none had a normal result with the thromboplastin-generation test.

Cases with even 1% antihæmophilic globulin in the plasma are likely to be clinically mild, and cases with a Bridge anticoagulant index over 2 are likely to be clinically severe; but exceptions to both these rules have been noted.

We are glad to acknowledge the constant help and cooperation we receive from Dr. E. Stratton, Dr. P. Renton, and the staff of the North-West Regional Blood Transfusion Service at Manchester; from Dr. H. Lempert and the staff of the department of clinical pathology at Manchester Royal Infirmary, and from the many other members of our own department. This work has been generously supported from their endowment funds by the board of governors of the United Manchester Hospitals.

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## Addendum

Since Jan. 1, 1961, the following new cases have been seen: 5 of classical hæmophilia, 2 of Christmas disease, and 1 of Hageman-factor defect.

# MYCOBACTERIAL SKIN ULCERS IN UGANDA

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NECROTISING skin ulcers, with undermined edges, have been seen over the past 3 years in patients attending Mulago Hospital in Kampala, Uganda. These ulcers have not responded to any simple form of treatment; and after a lengthy course, extending sometimes over 3 or 4 years, they cause severe disability. Similar ulcers were described by MacCallum et al. (1948) in 6 patients from Bairnsdale in Australia. The causative organism was found to be an acid/alcohol-fast mycobacterium, which was given the name *Mycobacterium ulcerans*. In the Congo a similar organism has been identified (Janssens et al. 1959), causing chronic ulcers with the same characteristics as those described by MacCallum and ourselves. The Congo ulcers were seen in a hundred and seventy patients grouped into 2 main geographical areas.

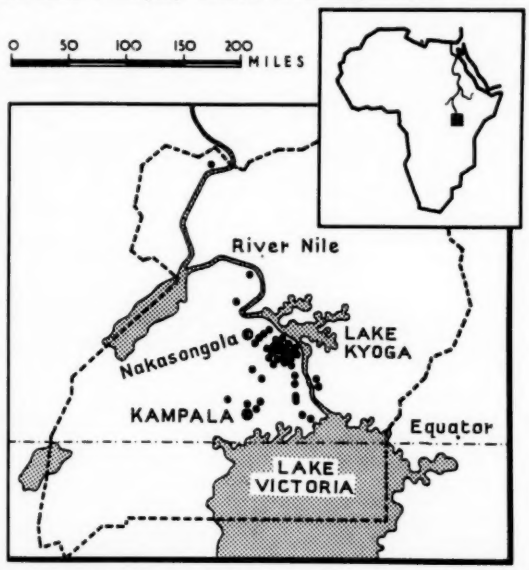


**Fig. 1—Map of Uganda, showing the homes of forty patients with mycobacterial ulcers, and the high incidence of this condition in the Buruli area.**

The patients in Uganda have come almost entirely from the district lying to the north and east of Kampala. Twenty-eight of the forty patients so far recorded live in a very limited area within the Mengo district, known as Buruli. This area has a low population density of less than fifty people per square mile, and it consists mainly of wild scrub near the southern bank of the Victoria Nile, where it flows through Lake Kyoga (fig. 1). No reason has yet been found for this high prevalence within a small area.

There is no predilection for any one African tribe to be affected; among the patients seen so far, nine tribes have been represented, and there is one Asian girl living near Buruli. The condition, however, tends to affect several members of the same family.

**Fig. 2—The forearm of a girl aged 13 (case 14), with an early lesion near the wrist, a larger one more proximally, and an established ulcer near the elbow.**

## Our Findings in Uganda

*Clinical Features* (H. F. L.)

The patients are usually children who are in good general health. The skin ulceration has usually been present for about 6 months before hospital treatment is sought. The history is often given of a minor injury to an exposed part of the body surface—e.g., a prick from a thorn or a sharp piece of wood. About 3 weeks later the indurated area remaining at this site extends in diameter and depth (fig. 2). At this stage the overlying skin is intact but more deeply pigmented than the normal surrounding skin. Although the lesion is not painful or hot, the patient usually seeks treatment at the local dispensary, and is often given penicillin by injection. Within the next few days the indurated skin begins to break down in the centre.

Once the skin surface is broken an ulcer forms with great rapidity, and a wide area of skin loss may result (fig. 3). Secondary infection ensues, and the ulcer floor soon becomes covered with foul-smelling granulations. The margins are irregular, with much undermining which extends sometimes 10–15 cm. beneath the edge. Such undermined skin feels indurated upon palpation and is

**Fig. 3—The abdominal wall of a boy aged 14 (case 13) in whom a wide area of skin became necrotic, leaving a huge ulcer with undermined edges.**

more deeply pigmented than normal skin. Buried in the ulcer floor and beneath the edges are masses of whitish necrotic material which, in chronic cases, becomes gritty and hard. The ulcer is usually single, but other small satellite ulcers may arise near the main one, separated only by bridges of undermined skin. In a few patients two or more of these ulcers have been in different parts of the body. The extensor surfaces of the arms and legs are most often affected, but lesions have also arisen on the chest, neck, abdomen, and scapular region. The regional lymphatic glands are not usually enlarged.

**Fig. 4—Gross contractures and scarring which have resulted from chronic ulceration of the hand and wrist in a girl of 6 years (case 20).**

The natural course of the ulceration varies. The ulcer may heal slowly over 6–9 months, often breaking down and extending on one side while skin is regenerating on another. Alternatively, the ulceration may extend widely, leading to gross deformities and contractures, so that amputation of a useless limb may have to be considered (fig. 4). But sometimes a small ulcer may persist for several years without such grave complications. In each case the patient's general health remains relatively unaffected by the presence of the ulcer.

The clinical findings in twenty-eight patients are indicated in the table.

*Special Investigations*

Radiological examination has revealed irregular areas of calcification in the soft tissues beneath most of the established ulcers. In two patients bone lesions have been found—in case 16 in the tibia adjacent to the skin ulcer, and in case 7 in the humerus and fibula on the opposite side of the body. Chest films have shown no evidence of pulmonary disease.

There have been no constant changes in the blood-picture or the blood-chemistry. Heaf or Mantoux testing of a proportion of the patients has given varying results (see table).

*Histopathology* (O. G. D.)

In one patient (case 14) a small non-ulcerated lesion (presumed to be early) was excised and sectioned. A wide area of necrosis was found in the dermis beneath intact epithelium. This area was acellular, consisting of homogeneous eosinophilic material, and no trace of collagen fibres remained. Within this necrotic area were found patches of calcification and large numbers of acid/alcohol-fast bacteria. Surrounding this area was a zone of scanty inflammatory reaction. A few neutrophil polymorphonuclears had penetrated a short distance into the necrotic tissue, and beyond these was a zone of mild lymphocytic infiltration. No giant-cell granulomata were seen.

In fully developed ulcers, the acellular necrotic area becomes surrounded by a well-marked chronic inflammatory reaction, with multinucleate giant cells. Sometimes a group of giant cells surrounds an amorphous foreign body. The ulcer floor is epithelialised by downgrowth from the adjacent epidermis. This epithelial hyperplasia is not only seen in the floor of the ulcer but also results in the overhanging margins of the ulcer being covered with epithelium on their deep surfaces. This layer of epithelium on the under surface of the ulcer edge, which delays natural healing, seems to be a unique feature of this type of ulcer.

The histological findings in our series are very like those described in the Congo ulcers by Janssens et al. (1959). The earliest observed change is an acute massive necrosis of the dermal collagen and subcutaneous fat. In twenty-eight of the forty cases so far collected, acid/alcohol-fast bacteria have been found in such necrotic areas. Because they are also present in the non-ulcerated early lesion, it seems unlikely that they are secondary invaders. Foreign material, on the other hand, has only been seen in ulcerated lesions, and may not be ætiologically important. The relatively banal inflammatory reaction appears to be a response to the presence of dead tissue, and giant cells do not appear in the early stage. The reactivity of the epidermis may reflect the fact that almost all our patients are children. The rapid epithelialisation of the ulcer floor accords with the tendency of these ulcers to heal spontaneously.

*Bacteriology* (J. K. C.)

The following is an account of the preliminary steps taken to identify the causative organism. Material is taken with a blunt curette, rather than with a cotton-wool swab, from beneath the overhanging edges of the ulcer, and it is examined as soon as possible after removal from the patient. In direct smears of pus, the organism is resistant to decolorisation with 3% acid-alcohol and 20% sulphuric acid, applied for 10 minutes. It

DETAILS OF TWENTY-EIGHT PATIENTS WITH PROVED ACID-FAST BACTERIA (A.F.B.) INFECTION

| Case no. | Sex | Age (yr.) | Site of lesion | Duration (mos.) | Period in hospital (mos.) | A.F.B. in pus | A.F.B. in tissues | Mantoux or Heaf test | Approximate size of ulcer (cm.) |
|---|---|---|---|---|---|---|---|---|---|
| 1 | M | 7 | Chest | 2 | 3 | — | + | + | 15 × 10 |
| 2 | M | 16 | Knee | 6 | 4 | — | + | — | 10 × 6 |
| 3 | F | 10 | Axilla | 1 | 3 | — | + | .. | 15 × 15 |
| 4 | M | 2 | Leg | 1 | 11 | — | + | .. | 12 × 40 |
| 5 | F | 10 | Neck | 1 | 6 | — | + | — | 8 × 3 |
| 6 | M | 14 | Wrist | 6 | 2 | — | + | + | 16 × 6 |
| 7 | M | 5 | Arm and hand | 12 | 7 | + | + | .. | 7 × 30 |
| 8 | M | 7 | Foot | ? | 3 | — | + | .. | 20 × 10 |
| 9 | F | 12 | Foot | ? | 4 | + | — | — | 15 × 8 |
| 10 | M | 2 | Leg | 6 | 2 | — | + | .. | 4 × 5 |
| 11 | M | 11 | Abdomen | 2 | 7 | + | — | .. | 10 × 8 |
| 12 | M | 10 | Foot | 6 | 4 | + | — | .. | 11 × 5 |
| 13 | M | 14 | Abdomen | 9 | 2 | + | + | .. | 45 × 25 |
| 14 | F | 13 | Arm | 3 | 2 | + | + | + | 6 × 5 |
| 15 | M | 7 | Arm | 6 | 3 | + | + | .. | 12 × 8 |
| 16 | M | 17 | Leg | 15 | 3 | + | — | .. | 18 × 6 |
| 17 | M | 60 | Leg and foot | 12 | 2 | + | — | .. | 5 × 7 |
| 18 | F | 8 | Hand | 1 | 6 | + | + | + | 4 × 3 |
| 19 | F | 19 | Arm | 3 | 3 | + | + | .. | 15 × 7 |
| 20 | F | 6 | Hand and leg | 12 | 6 | + | + | — | 20 × 6 |
| 21 | M | 18 | Shoulder | 2 | 1 | + | — | .. | 9 × 7 |
| 22 | F | 7 | Shoulder | 1 | 4 | — | + | .. | 8 × 8 |
| 23 | F | 9 | Chest | 2 | 3 | — | + | .. | 19 × 12 |
| 24 | M | 6 | Chest | 1 | 2 | + | + | — | 8 × 4 |
| 25 | M | 60 | Leg | 1 | 1 | + | — | .. | 15 × 10 |
| 26 | F | 28 | Leg | 3 | 3 | + | + | + | 9 × 6 |
| 27 | F | 30 | Leg | 2 | 3 | + | + | + | 14 × 11 |
| 28 | F | 5 | Ankle | 36 | 4 | + | — | — | 9 × 7 |

fluoresces when stained with auramine and when subjected to ultraviolet light. It is gram-positive when the crystal violet is warmed. The organisms appear in clumps, singly or in pairs, and when in clumps, they are often parallel to each other. In direct smears of pus 70% of these clumps are extracellular. The average size of the organism is 2·1–2·8 μ by 0·28–0·33 μ. The number of bacilli in a clump sometimes exceeds 100, but the average number is 16. Some beading has been noted but no spores or capsules have been found.

Culture of the organism has been slow and difficult. Tissue is suspended in Ringer's solution, treated with sodium hydroxide, and centrifuged. The deposit is washed and inoculated on to sets of several media at various temperatures. Those of Petragnani and Löwenstein-Jensen have proved most successful. Acid/alcohol-fast bacteria have been isolated on these media after 7 weeks' incubation at 33°C on twelve occasions, the material having been taken from five patients. The general appearance of the colonies after 7 weeks is: 2–3 mm. in diameter; low and convex; pale cream in colour; and somewhat moist. No growth has yet been obtained at room temperature (about 25°C) or at 37°C, even after as long as 6 months' incubation of the primary culture.

Subcultures were made on Löwenstein-Jensen and Petragnani media with a standard inoculum. Profuse growth was obtained at 33°C, but incubation at 37°C yielded a few minute colonies, and only two of forty-five subcultures incubated at 25°C showed any trace of growth. The growth obtained at various temperatures is comparable, because a standard inoculum is used for all subcultures. The addition of an extract of *Myco. tuberculosis* var. *humanis* does not enhance the growth of this organism. Growth is also evident on Dorset's medium, but this is not so profuse as on the above media. Only a few colonies grew on oleic-acid/albumin medium. Subcultures require at least 3–4 weeks' incubation to give profuse growth. Ziehl-Neelsen staining of 60% of the colonies so far isolated shows a tendency towards clumping similar to that described above.

Cultural characteristics suggest an organism resembling *Myco. ulcerans* or an allied mycobacterium. The bacilli isolated to date bear no resemblance to human, bovine, or avian types of *Myco. tuberculosis*, or to *Myco. lepræ*. Further subcultures, sensitivity tests, and animal inoculation experiments are in progress.

## Treatment

No specific remedy has yet been found to influence the progress of these ulcers. Streptomycin and isoniazid have been given to the majority of the patients for periods of 1–12 weeks, without clear evidence of clinical improvement, but on three occasions these drugs have contributed to the healing of recurrent ulceration. Usually dapsone given for 3 months or more seems to improve their condition. Tetracyclines have proved the most effective means of controlling secondary infection.

In practice, the ulcer surface has been cleaned up most rapidly by the use of dry dressings during the initial course of antibiotic therapy after admission to hospital. Moist saline dressings are sometimes used for small children. The patient is prepared for operative treatment as soon as secondary infection is controlled. Under general anæsthesia (with a tourniquet if applicable) all necrotic tissue is excised, together with the ulcer margin, until normal skin and subcutaneous tissues are reached. A small piece of this excised tissue is sent for biopsy, and all the remaining debris is placed in a dry sterile vessel for bacteriological study by smear and culture. The excision cannot always be complete, because of anatomical barriers such as nerves and blood-vessels. In that event the structures remaining are cleared of necrotic material as far as possible with a blunt curette. The raw area remaining after the excision is covered with split-skin grafts. If, through partial failure, these do not provide a complete cover, further skin grafts are applied within 10 days. At the same time, if joint contractures are present, these are gradually corrected by changes of plaster cast.

## Discussion

Reference has already been made to the reports of MacCallum et al. (1948) and Janssens et al. (1959), which describe necrotising skin ulcers from which acid/alcohol-fast bacilli were recovered. There are certain minor differences in the clinical features and in the characteristics of the organisms which suggest that mycobacteria allied to *Myco. ulcerans* may be responsible for these Uganda ulcers.

In particular, organisms from our patients are mainly extracellular in direct smears. At first it was difficult in Uganda to produce lesions in laboratory animals, although culture had proved that the inocula used were viable. *Myco. ulcerans* has been studied very carefully by Fenner and Leach (1952) and Leach and Fenner (1954) and by Fenner (1956, 1957) in relation to allied organisms such as *Myco. balnei*, *Myco. ranæ*, and *Myco. phlei*, but none of these corresponds exactly to the organism found in Uganda.

An organism similar to *Myco. ulcerans*, but not identical, was reported by Norden and Linell (1951) in Sweden to have caused ulcers, the infection being contracted in swimming-baths. Various allied mycobacteria known to have caused disease in animals and man were reviewed by Francis (1958). Wells et al. (1955) describes lesions due to *Myco. fortuitum*; but this organism, like so many of its kind, grows much more freely and at a greater range of temperature than the Uganda variety.

Several necrotising skin ulcers have been reported in man apart from those found in Australia and the Congo. The one most similar to ours is that described by van Oye and Ballion (1950) in West Africa, but this has not been confirmed in the laboratory. Lavalle et al. (1953) reported the case of a farmer in Mexico with an ulcer of the hand which was thought to be due to *Myco. ulcerans*.

The general picture suggests that an acid/alcohol-fast mycobacterium, either *Myco. ulcerans* or an allied organism, is responsible for severe and chronic skin ulceration in several parts of the world. At present no specific treatment can be offered, apart from radical excision of all abnormal tissue. Acid/alcohol-fast bacteria are not always recognisable in the pus or granulation tissue of the ulcer base, and they may be present only in the recesses of the overhanging ulcer edge. Because the organism is sensitive to changes in temperature, it only grows at 33°C in primary culture. Facilities for this type of incubation are not always available, and this may account for past failures to culture the organism when incubation has been at room or body temperature.

There are many possibilities as to how these mycobacteria reach the subcutaneous tissues. Apart from local trauma due to minor puncture wounds, there is the possibility of some form of insect or other animal vector conveying infection. The area in which most of our patients live is infested with various types of biting fly. The soil in and around the houses teems with hookworm ova, the larvæ from which could infect simultaneously wide areas of skin in contact with the ground. Houseflies could transmit organisms from infected cattle and domestic animals.

One of the most striking features in our series is the absence of serious systemic effects of gross ulceration. This feature is common to all reports of similar disease elsewhere. It was the opinion of Janssens et al. (1959) that the acute necrosis, very slight inflammatory reaction, and absence of systemic illness are the result of a local tuberculin type of hypersensitivity, perhaps to a product of the invading mycobacteria. On the other hand, most of these patients are so young that there might not have been time

for such a degree of resistance to be developed. The lesions could therefore be explained by the local toxic effect of organisms embedded deeply in the subcutaneous fat.

Non-tuberculous mycobacteria have recently been identified in lesions of the lung (Christianson and Dewlett 1960), and in various other tissues (Weed 1956). The part played by atypical mycobacteria in disease of man is thus becoming better appreciated, especially in relation to the significance of skin-testing. We hope that further study will be possible in this direction, and also towards completing the identification of the causative organism.

**Summary**

Chronic necrotising skin ulcers of an unusual type arise, mainly in children, in a small district in Uganda. Forty such patients have been seen, and in twenty-eight, acid/alcohol-fast organisms have been identified.

The organism, which has been grown in primary culture at 33°C, may be *Myco. ulcerans* or a related species.

The only effective treatment is radical excision and skin grafting.

The source of the infection is as yet unknown. Similar mycobacterial ulcers have been described in Australia, Mexico, and the Congo.

Our thanks are due to Prof. I. W. J. McAdam, for permission to report the details of patients under treatment at Mulago Hospital; to Prof. J. N. P. Davies, for his interest and cooperation; to Dr. A. M. M. Wilson, for recognising the type of organism concerned in 1959; to the department of medical illustration; and to Mr. Robert Tunnicliffe, F.I.M.L.T., for technical assistance. Dr. J. James has helped with the references. The work was aided by funds provided by the Makerere College research grants committee.

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# POSTOPERATIVE IRRADIATION OF CORNEAL GRAFTS

## ITS POSSIBLE EFFECT ON THE IMMUNOLOGICAL REACTION

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TRANSPLANTATION of an organ from one individual to another has almost always proved unsuccessful. The single exception to this is the cornea, where the grafted tissue can be expected to survive and remain healthy. As a rule, only the central portion of the cornea is transplanted. The usual diameter of such a partial graft is from 5 to 8 mm., which means that the donor material lies within a ring of host cornea.

Where the recipient cornea is completely avascular—e.g., in keratoconus—a technically perfect partial graft will always remain clear. On the other hand, a total penetrating graft, where the donor material is inserted directly into the vascular sclera, will, with equal certainty, become opaque. Furthermore, even a technically perfect partial penetrating corneal graft may become opaque if the host cornea is vascularised as a result of previous disease, since in such a case blood-vessels may enter the donor tissue. Indeed, the commonest cause of failure of a technically successful corneal graft is vascularisation, followed by an immunological reaction. Homografts of skin and other vascularised tissues are rejected as a result of an antigen-antibody reaction following the growth of blood-vessels from the host into the transplanted tissue (Merwin and Hill 1954).

Though the cornea is antigenically active, a corneal homograft will not show a clinical immune response unless it becomes vascularised. In these cases the initial vascularisation of the graft takes place during the healing process: small vessel buds grow from the cut ends of numerous arterioles in the host cornea. However, once a few vessels have entered the graft it becomes œdematous throughout and innumerable leashes of vessels grow in from all round the periphery, indicating a generalised response within the transplanted tissue. Such an immunological reaction is characteristic and easily recognised. The œdema leads to thickening of the stroma and a ground-glass appearance of the epithelium. Numerous active leashes of blood-vessels are visible in the substantia propria. As the acute phase passes, fibrosis and permanent opacity result.

If in the earliest stage of the allergic response intensive local corticosteroid treatment is applied, the condition may be controlled. But this is by no means certain; and in any event there is likely to be recurrence when the steroid is withdrawn.

### Effects of Irradiation

The observation that entry of blood-vessels into the graft almost certainly spells failure has led to attempts to find other methods of control.

Castroviejo (1943, 1945) advocated radiotherapy for the control of vascularisation following keratectomies and keratoplasties. Newly formed blood-vessels are relatively radiosensitive, and, if applied early enough, irradiation should destroy them and thereby prevent the graft from becoming opaque. It was with this direct action in mind that we started using radiotherapy for early vascularisation in corneal grafts. In 3 of the early cases treatment was with superficial X rays, but in the remainder we have used a beta-ray applicator containing strontium 90. This instrument is applied directly to the corneal surface or held just in front of it (Ainslie 1961, Ainslie, Snelling, and Ellis 1961).

The table shows the clinical results, which have been excellent. In all cases when the treatment started open blood-vessels could be seen in the graft, and they were increasing in size and in number, despite intensive use of corticosteroids. Corticosteroid treatment was continued during the irradiation therapy.

After the radiotherapy, the initial and secondary blood-vessels retrogressed in all cases and graft œdema disappeared in all but 1 (case 10). In 13 the blood-vessels disappeared entirely, while in 3 a few vessels remained (cases 1, 10, and 14). In case 1 the cornea has become completely clear but in the two others some opacity persists.

These results show the value of beta-irradiation as a practical means of controlling vascularisation of corneal grafts. If started early enough, it will nearly always prevent opacity caused by vascularisation; and this allows the surgeon to perform a primary penetrating corneal graft in a vascularised cornea with every hope of success. There is no longer need for one or more preliminary lamellar grafts, designed to reduce the vascularity of the host cornea.

### Mode of Action

That radiotherapy is clinically effective seems certain but its mode of action remains in doubt. The nature of the response to irradiation suggests that it may not be due entirely to direct destruction of the newly formed blood-vessels by the beta-rays. Though the dose of radiotherapy is small, the regression of the vessels is very rapid, and in some cases the œdema disappears before all the blood-vessels are empty. Indeed, in case 1 blood-vessels have remained permanently open for nearly two years, yet the graft has remained clear. It is true that new blood-vessels often grow into injured or diseased corneæ, and that these vessels may be reduced by radiotherapy. Here, however, the response is slow, and the doses required are much larger than in our postoperative cases. It seems possible, therefore, that the radiotherapy modifies the immunological reaction.

Our evidence suggests that damage to the grafted donor cornea is due to a local rather than a general immune reaction on the part of the host. Probably, this consists only of the response of the recipient to the antigens in the donor cornea, and the latter contains no cells or antibodies capable of reacting to the antigens of the host. If this is so, there need be no concern about the possible reaction of the donor cornea to the host's antigens.

Our present hypothesis is that mesenchymal cells, capable of reacting with the antigens of the donor cornea, grow into the grafted tissue with the blood-vessels. Corticosteroids depress this reaction but do not destroy the cells, and the condition will therefore recur when the steroids are withheld. If the cells are destroyed by irradiation, however, the reaction cannot take place. This suggests that fixed antibody may be responsible for the reaction.

If this possibility can be confirmed, it may have application beyond keratoplasty. Hitherto our observations have been entirely clinical, but we are now following them up experimentally. A great advantage of the corneal-graft technique in experimentation is that the reactions to the graft can be observed directly and recorded photographically.

### Summary

Beta-irradiation completely controlled vascularisation in 13 out of 16 corneal grafts.

TABLE OF TREATMENT AND RESULTS

| Case no. | Condition necessitating graft | Previous keratoplasties | Operation performed | Total dose of irradiation | Postoperative day of start of irradiation | Previous irradiation to cornea | Results | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | Clarity of grafts | State of vessels |
| 1 | Interstitial keratitis | Two penetrating grafts (cornea remained opaque and vascularised) | 7·1 mm. penetrating graft | 1200r* | 21 | Nil | Clear | A few open vessels remain |
| 2 | Disciform keratitis | Nil | 7·0 mm. penetrating graft | 1200r* | 40 | Nil | Clear | No vessels remain |
| 3 | Dendritic nebulæ | Nil | 6·0 mm. penetrating graft | 1800r* | 42 | Nil | Clear | No vessels remain |
| 4 | Disciform keratitis | Nil | 6·0 mm. penetrating graft | 400r | 21 | Nil | Clear | No vessels remain |
| 5 | Interstitial keratitis | One lamellar and two penetrating grafts (cornea remained opaque and vascularised) | 5·5 mm. penetrating graft | 1000r | 21 | Nil | Clear | No vessels remain |
| 6† | Interstitial keratitis | Nil | 6·0 mm. penetrating graft | 1000r | 16 | Nil | Clear | No vessels remain |
| 7 | Caustic burn | Nil | 6·0 mm. penetrating graft | 500r | 12 | Nil | Clear | No vessels remain |
| 8 | Corneal ulceration (leucoma) | Nil | 7·0 mm. penetrating graft | 500r | 22 | Nil | Clear | No vessels remain |
| 9 | Disciform keratitis | 6·0 mm. penetrating graft (cornea opaque; extensive anterior synechia) | 7·5 mm. penetrating graft | 900r | 48 | 950 (SXR) 3 years previously | Clear | No vessels remain |
| 10 | Corneal ulceration (leucoma) | Nil | 7·0 mm. penetrating graft | 1000r | 28 | Nil | Corneal œdema —lower periphery | A few leashes of vessels below |
| 11 | Disciform keratitis | Nil | 6·0 mm. penetrating graft | 500r | 23 | Nil | Clear | No vessels remain |
| 12 | Trachoma | Nil | 7·0 mm. penetrating graft | 500r | 21 | Nil | Nebula below (remainder clear) | No vessels remain |
| 13 | Rosacea keratitis | 7·0 mm. penetrating graft (anterior synechiæ and vascularisation) | 8·0 mm. penetrating graft | 1000r | 23 | Nil | Nebula and anterior synechia above (remained clear) | No vessels remain |
| 14 | Trachoma | Nil | 5·5 mm. penetrating graft | 500r | 21 | Nil | Nebula upper periphery of graft | Superficial vessels in upper periphery |
| 15 | Interstitial keratitis | One lamellar graft heavily vascularised) | 5·5 mm. penetrating graft | 1000r | 24 | Nil | Clear | No vessels remain |
| 16 | Vascularised degenerate central cornea | Nil | 6·1 mm. penetrating graft | 1000r | 21 | Nil | Clear | No vessels remain |

* Superficial X-rays used in these cases. Irradiation in all other cases by strontium-90 plaque (beta-irradiation) 400–500r was given initially: if necessary a second application was made 5–7 days later.

† Case 6 is the fellow eye of case 5.

In many cases requiring grafts, irradiation obviates the need for preliminary keratoplasty undertaken to reduce the vascularity of the host cornea.

Irradiation may work partly by modifying the immunological reaction.

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# DIFFERENTIAL TRANSMISSION OF DOWN'S SYNDROME (MONGOLISM) THROUGH MALE AND FEMALE TRANSLOCATION CARRIERS

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INHERITANCE of Down's syndrome through translocations involving chromosome no. 21 and one of the other acrocentric chromosomes (13–15, 22, Denver) are now well known.

In families where the anomaly has been transmitted by a 13–15/21 ($D/G_{21}$)* translocation, the carriers have all been female, whereas in cases of 21/21 or 21/22 ($G/G_{21}$) type the carriers have all been male (Fraccaro et al. 1960, Forssman and Lehmann 1961, Hamerton et al. 1961). There have been reports of a female carrier with a $G/G_{21}$ type translocation (Hamerton et al. 1961) and a male carrier with a $D/G_{21}$ type translocation (Forssman and Lehmann 1961); but in the latter case the boy was only six years old and was not, of course, proven fertile and therefore capable of transmitting the anomaly. Recently we have had the opportunity of studying the chromosomes of a large family in which a $D/G_{21}$ translocation has been transmitted by both phenotypically normal male and female carriers.

* The classification of the chromosome groups proposed by Patau et al. (1960) will be used, because it is simpler in designating translocations between chromosomes of different groups.

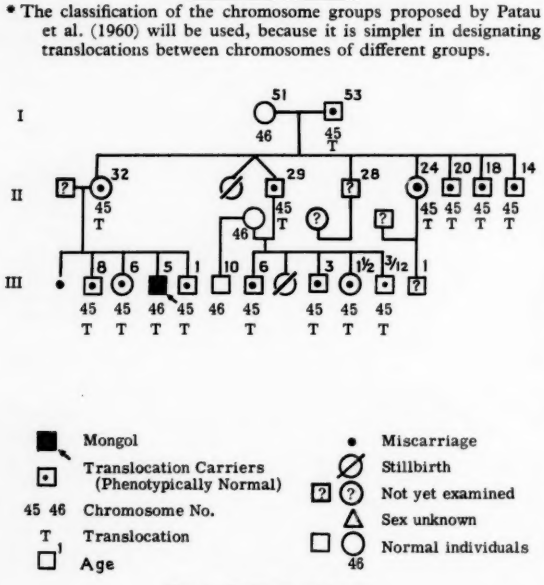


**Fig. 1—Pedigree of family.**

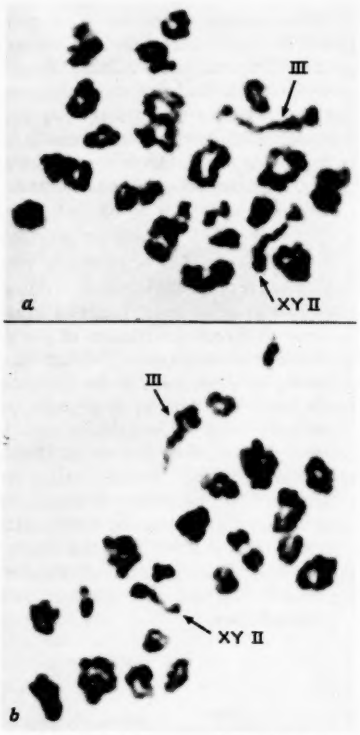


**Fig. 2—II-5. Chromosomes of two primary spermatocytes in diakinesis of the first meiotic division. 22 bodies, ($20^{II}$ $1^{III}$ $XY^{II}$). (X2285, reduced from ×4000, Feulgen stained.)**

## Findings

*The Family*

The pedigree is shown in fig. 1. The propositus (III-4), a five-year-old boy affected with Down's syndrome, was found to have 46 chromosomes and to carry a typical $D/G_{21}$ translocation. Examination of his mother (II-2), a phenotypically normal female, revealed 45 chromosomes and a similar translocation. The cytological and other data in the remainder of this family are summarised in fig. 1. The karyotypes of the translocation carriers are identical with those reported in other families of this type (Penrose et al. 1960, Carter et al. 1960). There are 45 chromosomes, with an additional chromosome in the X-6-12 group, and one less in the 13-15 and 21-22 groups. The one patient with translocation Down's syndrome has 46 chromosomes with a similar karyotype to the carriers, but with the full complement in the 21–22 group.

*Meiotic Studies*

A testicular biopsy was performed on the uncle of the propositus (II-5) in order, first, to confirm that the abnormal chromosome resembling a member of the X-6-12 group resulted from a translocation, as had been strongly inferred in the past (Polani et al. 1960, Penrose et al. 1960, Carter et al. 1960), and secondly to attempt a direct analysis of the pairing and segregation of this chromosome.

In brief, seminiferous tubules were removed by biopsy, divided into two portions, and pretreated, one half with hypotonic sodium citrate and the other with hypotonic saline. They were fixed in acetic alcohol, and stained with Feulgen's reagent. Squash preparations were then made. A small biopsy specimen was also immediately fixed in Bouin's fluid for conventional histology.

TABLE I—CHROMOSOME CONSTITUTION OF PRIMARY SPERMATOCYTES AT FIRST DIVISION OF MEIOSIS IN A 45 CHROMOSOME TRANSLOCATION CARRIER (II–5)

| Number of bodies | <22 | 22 | 23 | | 24 | Total |
|---|---|---|---|---|---|---|
| | | $20^{II}\,XY^{II}\,1^{III}$ | $20^{II}\,X^{I}\,Y^{I}\,1^{III}$ | $20^{II}\,XY^{II}\,1^{uni}+1^{I}$ | $21^{II}+3^{I}$ | |
| Number of cells .. | 4 | 30 | 11 | 1 | 2 | 48 |

I Univalent. III Trivalent.
II Bivalent. uni Unequal bivalent.

Fig. 2 shows two typical plates in diakinesis. Twenty-two bodies can be seen. Detailed analysis shows that they consist of twenty-one bivalents (including the unequal sex bivalent) and one trivalent. Other types of association observed in a few cells were three univalents and (in one cell) one univalent together with one unequal bivalent. The frequency of these different types of chromosome association is shown in table I.

Examination of second metaphase plates was not entirely successful, owing to difficulties in obtaining good well-fixed chromosomes at this stage.

## Discussion

The presence of a trivalent, at diakinesis and first metaphase, in the majority of primary spermatocytes confirms that the abnormal chromosome results from a reciprocal translocation between two acrocentric chromosomes, as was originally suggested (Polani et al. 1960, Penrose et al. 1960, Carter et al. 1960).

A trivalent of this type has four possible disjunctional arrangements, each resulting in two complementary classes of gametes (fig. 3). Thus an individual heterozygous for such an interchange can produce eight cytologically distinct classes of gametes (fig. 3). Three of these (*1a*, *1b*, and *IIa*) are known, and one (*IIb*) is inferred from the study of the children of $D/G_{21}$ translocation carriers (Penrose et al. 1960, Carter et al. 1960). The latter would result in a zygote monosomic for chromosome number 21, which would probably be lethal.

The present family differs from the two $D/G_{21}$ families previously reported (Penrose et al. 1960, Carter et al. 1960) in that the translocation is transmitted through both male and female carriers, and it is noticeable that where there were children affected with Down's syndrome (Penrose et al. 1960, Carter et al. 1960, Buckton et al. 1961, Forssman and Lehmann 1961) (also in this family) the transmission of the translocation has always been maternal.

DISJUNCTIONS AND GAMETIC TYPES FROM A $D\text{-}G_{21}$ TRANSLOCATION

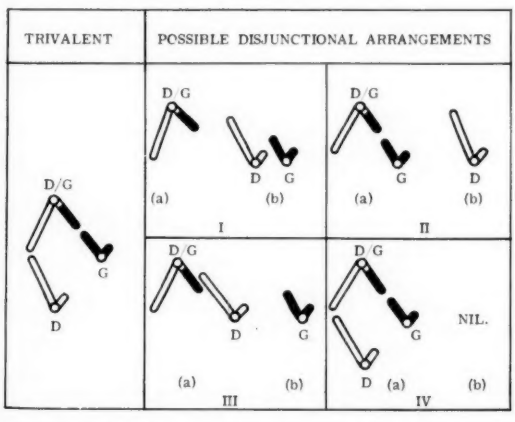


**Fig. 3—Possible disjunctional arrangements of a $D/G_{21}$ translocation.**

Comparison of the available data on the classes of children produced by male and female carriers (table II) suggests that, although the numbers are small, there is a real difference between the maternal and paternal transmission ratios, and further that, within each sex, the ratios depart from equality, as would be expected on the basis of mendelian segregation. In fact, a comparison of the number of carriers and normal individuals produced, gives a $\chi^2$ value of 8·1 for male and 10·56 for female transmitters ($P > 0{\cdot}001$), a significant departure from random segregation.† Comparison of the numbers of affected and carrier progeny of female transmitters is more difficult because of the ascertainment bias in these families. However, removal of the propositi from these six families leaves six affected children to be compared with fifteen carriers ($\chi^2 = 3{\cdot}04$ $P < 0{\cdot}05$). A comparison of affected and carrier progeny of male transmitters gives a $\chi^2$ value of 8·1 ($P > 0{\cdot}001$).

TABLE II—COMPARISON OF NUMBERS OF CHILDREN PRODUCED BY MALE AND FEMALE TRANSMITTERS

| Sex of carrier | No. of carriers | Children of carriers | | | | Total |
|---|---|---|---|---|---|---|
| | | Affected | Carriers | Normal | Not known* | |
| ♀ | 8 [1] | 12 | 15 | 1 | 11 | 39 |
| ♂ | 2 [2] | Nil | 11 | Nil | 2 | 13 |
| Total | | 12 | 26 | 1 | 13 | 52 |

1. Penrose et al. 1960. Buckton et al. 1961. Miller and Breg 1961. Carter et al. 1960. Forssman and Lehmann 1961.
2. Present family.
* Including deaths, miscarriages, &c.

Thus, even allowing for the bias due to selection, it seems clear that affected offspring are apparently *not* produced by male but *are* produced by female transmitters. If this is so, there are two possible explanations. Firstly, the trivalent may orientate differently on the metaphase plate in male and female meiosis, resulting in the formation of different classes of gametes with varying frequency; or secondly, the different classes of spermatozoa formed by a male carrier may differ in their fertilising efficiency.

The observed results could perhaps best be explained by a combination of preferential segregation and selective fertilisation. For instance the favouring of types *1a* and *IIa* gametes (fig. 3) in females, but only of type *1a* (fig. 3) in males, or alternatively, if the disjunctional arrangements are identical in both sexes, then selection must be operating amongst the gametes. A system of gametic selection is difficult to visualise between different classes of ova; more likely perhaps in the female is a meiotic system favouring recovery of the translocated chromosome. A system of this type has in fact been described by Zimmering (1955) for certain translocations in Drosophila. In males preferential segregation may also be operating, but in that sex the possibility of gametic selection is much greater.

The evidence for selective fertilisation in mammals has been reviewed by Braden (1960) and need not be elaborated here. There is, however, some evidence of selective fertilisation in the mouse, based on abnormal segregation ratios of alleles at the T locus (Braden 1958, 1960, Bateman 1960), although the maternal genotype seems to be concerned to some extent in this.

In the present family, the progeny of the two male carriers (I-2 and II-5) are all translocation carriers, suggesting that sperm of type *1a* only is successful in effecting fertilisation. Type-I disjunction, however, produces two complementary types of sperm (1a and 1b), unless some form of preferential segregation is operating

† We are indebted to Dr. Fraser Roberts for discussing the statistical problems involved here. The formula for $\chi^2$ used when expectation in equality is $\chi^2 = \frac{(\text{Difference} - 1)^2}{\text{No. of observations}}$.

in favour of recovery of the translocated chromosome so that only Ia spermatozoa are formed. If this is so then we must also postulate only type-I disjunctions occurring in males. More likely perhaps in males, if we assume that haploid gametes are capable of phenotypic expression (this is necessary if any form of selection is to act), is a situation where two or more cytologically different classes of sperm are available for fertilisation: this rules out preferential selection of one type of sperm by the genotype of the ovum, as seems to happen at the T locus in mouse (Braden 1960). Contrary to expectation, however, only chromosomally abnormal zygotes appear to be produced. The possibility that the missing classes of zygotes are lethal is ruled out, as some of these zygotic types are formed after maternal transmission though with aberrant frequencies. A more likely explanation is that the *Ia* class of spermatozoa has a very strong selective advantage, at least over the *Ib* class, and perhaps over the other classes if formed. Both of these classes of spermatozoa are cytologically balanced and they differ from each other only by the deficiency of a minute centric fragment in class *Ia*. The significance of this is not clear, but it could logically be the reason for the apparently advantageous phenotype shown by this class of sperm.

The possibility that this finding has a general application to the transmission of translocation Down's syndrome and its carrier state is suggested by the fact that the high mean maternal age at the birth of children with the syndrome is *not* lowered when familial Down's syndrome is transmitted through the father—in contrast with the situation when transmission is maternal (Penrose 1951). Besides receiving some support from this difference, our finding also offers an explanation for it: when Down's syndrome is found among the paternal collaterals of the patient, this could be due in some instances to a chance familial concentration, in others to translocation transmission (or possibly some other inheritable mechanism). If our finding had a general validity, the appearance of Down's syndrome among the children of " transmitter " males should be related to the ordinary mechanism of production of the condition, and consequently correlated with advancing maternal age. This in fact seems to be the case.

Finally, if these conclusions are correct, then not only must our ideas on the mode of inheritance of these translocations and the frequencies of the different classes of progeny of transmitters be changed, but also it would seem to be the first occasion that selective fertilisation, preferential segregation, or both, have been demonstrated in man.

**Summary**

A family is described in which a $D/G_{21}$ translocation is transmitted by both male and female carriers.

Evidence is presented suggesting that there may be differential transmission of the chromosome types between the two sexes, and furthermore that cytologically differing classes of sperm produced by male carriers may vary in their efficiency in effecting fertilisation.

Our thanks are due to this family for their cooperation in this investigation—particularly to the uncle of the propositus who consented to a testicular biopsy. We should also like to thank the surgeon Mr. F. Ellis, who carried out this operation, and Dr. B. Kirman for access to the propositus who is under his care. We are indebted to Miss A. Horsley and Miss V. M. McGuire for their expert technical assistance.

*References at foot of next column*

# ATYPICAL CASES OF SALMONELLOSIS IN HOSPITAL

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RECENTLY I have been impressed by a number of atypical cases of salmonella infection in the Radcliffe Infirmary, and this paper records briefly their clinical features. The proportion of atypical forms among sporadic cases of salmonellosis in hospital seems to be much higher than among cases of the disease in general.

## The Patients

Between July, 1956, and August, 1960, 76 cases of salmonella infection were admitted to the hospital or appeared among inpatients. 33 of them were due to *Salmonella senftenberg*, and they will not be further considered because no complications arose, and these can easily be separated from the sporadic cases.

SALMONELLA INFECTIONS IN THE RADCLIFFE INFIRMARY FROM JULY, 1956, TO AUGUST, 1960

| Organism | No. of cases | Remarks |
|---|---|---|
| *S. paratyphi* B .. | 5 | Including cases 3, 4, and 5 |
| *S. typhimurium* .. | 30 | Including cases 7, 8, and 9, and an outbreak of 20–25 cases |
| *S. heidelberg* .. .. | 1 | Case 2 |
| *S. schwartzengrund* .. | 1 | .. |
| *S. newport* .. .. | 1 | Case 6 |
| *S. bovis-morbificans* .. | 1 | .. |
| *S. typhi* .. .. | 1 | .. |
| *S. enteritidis* .. .. | 1 | .. |
| *S. dublin* .. .. | 1 | Case 1 |
| *S. anatum* .. .. | 1 | .. |
| *S. senftenberg* .. | (33) | Not included among sporadic cases |

The other salmonella serotypes are shown in the table. The following are brief records of the clinical features of 9 unusual cases:

**Case 1.**—A man of 57, with long-standing myelosclerosis, was admitted to hospital for splenectomy because he was found to be destroying transfused red cells at an increasingly rapid rate. He was pyrexial (102·4°F) and had felt hot and dizzy for two days. There were no localising physical signs, but *S. dublin* was isolated from blood cultures, though never from either fæces or urine. The patient was treated and he became apyrexial; but after six weeks his temperature rose again to 102°F, he had a rigor, and he complained of pain over the spleen. Despite sterile blood cultures he was given further treatment, and he was apyrexial when discharged. Later he was readmitted for splenectomy, feeling well. At operation a very large spleen (2680 g.) was removed with difficulty, partly because it contained a large abscess. The patient died shortly afterwards from uncontrollable intra-abdominal hæmorrhage. *S. dublin* was isolated from the splenic abscess and also from a postmortem blood culture, but it could not be cultured from the fæces.

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**Case 2.**—A woman, aged 71, had for some years had recurrent attacks of strangulated femoral hernia; at last symptoms of small-intestinal obstruction had developed, and she was admitted as an emergency. At operation the obstruction was found to be due to old adhesions which were freed. Five days later pus began to discharge from the abdominal wound, and *S. heidelberg* was isolated. The same organism was later found in the fæces and urine. Blood culture was not done. She was constipated throughout the illness.

**Case 3.**—A man of 61, admitted with colicky upper abdominal pain, and vomiting, gave a history of attacks of pain, associated with jaundice, going back for thirty years. On admission he was shocked, with a temperature of 97·6°F, and generalised tenderness in the right upper quadrant of the abdomen. Two days later his temperature rose to 102°F, and jaundice and diarrhœa appeared. *S. paratyphi* B was isolated from his fæces. A cholecystogram later showed a non-filling gallbladder. When the patient was readmitted for cholecystectomy, *S. paratyphi* B was isolated from the bile, while the gallbladder showed chronic cholecystitis and cholelithiasis.

**Case 4.**—A man of 56 was admitted with a story suggestive of carcinoma of the colon; at operation he was found to have a mucoid adenocarcinoma of the transverse colon, and transverse colectomy was performed. Ten days later severe pain developed in the right iliac fossa, his abdomen became distended, and his temperature rose to 104·4°F. Laparotomy was performed, revealing multiple adhesions and free thin pus in the pelvis. The adhesions were divided and the pelvis was drained. *S. paratyphi* B was isolated from the pelvic pus. Three days later he started to have diarrhœa, and *S. paratyphi* B was grown from the fæces.

**Case 5.**—A young woman of 26 gave a ten-day history of vulval ulceration. Two days before admission she had had a short bout of generalised abdominal pain which had recurred next day, together with some diarrhœa. She was febrile (99·4°F) and showed generalised guarding of the lower abdomen. There were two shallow ulcers on the inner aspects of the labia minora, and another in the posterior fornix. An indefinite mass could be felt in the pelvis. Blood and urine cultures were sterile, but from the fæces and also from a high vaginal swab, *S. paratyphi* B was isolated. At posterior colpotomy a large amount of foul pus was obtained from which *S. paratyphi* B was isolated. She was later readmitted for a further colpotomy. This time 6 oz. of clear sterile fluid was obtained, and a specimen of fæces yielded no pathogenic organisms.

**Case 6.**—A young man of 28 had chronic agranulocytosis. He had had a series of infections, and two years before his final admission to hospital a large inflammatory mass appeared in the right iliac fossa. This had yielded to treatment, but it had recurred seven months later, and again nine months after that. He was apyrexial, but his abdomen was distended, and there was a tender diffuse mass on the right. He had a very large spleen, and almost complete agranulocytosis. *S. newport* was isolated from the fæces. After treatment this organism disappeared, and it was decided to operate. A large abscess opening into the hepatic flexure was found in the right loin; this was drained and splenectomy and right hemicolectomy were performed. Pus from the abscess cavity was sterile. The spleen showed amyloid disease, and the patient died very shortly with an *Escherichia coli* septicæmia.

**Case 7.**—A woman of 61 gave a two-week history of profuse offensive vaginal discharge, anorexia, and lower abdominal pain. She had vomited once, and diarrhœa had begun before admission to hospital. She was pyrexial (101°F), and had a poorly defined tender firm mass in the pelvis. A profuse yellow-brown vaginal discharge was found to be coming from a sinus in the posterior fornix. *S. typhimurium* was isolated from this discharge and from the fæces. Treatment produced great improvement in her general condition, and two months later she was symptom-free although *S. typhimurium* was still present in the fæces and there was still a pelvic mass.

**Case 8.**—A man of 21 gave a thirty-hour history of colicky lower abdominal pain. He vomited once but had no diarrhœa. He was pyrexial (100°F), with tenderness, guarding, and rebound tenderness at the mid-point of the spino-umbilical line. Appendicectomy was performed, but the appendix was normal. Two days later he passed four loose motions, and *S. typhimurium* was isolated from the fæces.

**Case 9.**—A man of 26 had had, for twenty-four hours, central abdominal pain of gradual onset, associated with nausea and diarrhœa. He had a temperature of 101·4°F, and the right iliac fossa was tender, with guarding, rebound tenderness, and hyperæsthesia. At operation a normal appendix was found, but the lower ileum looked inflamed and the abdomen contained a little clear fluid. Two days later *S. typhimurium* was isolated from the fæces.

## Discussion

Cases of salmonella infection arising sporadically in hospitals are more likely to present atypically than those seen in general practice. In this series 7 (i.e., 16%) of the 43 sporadic cases seen in the Radcliffe Infirmary during the four years 1956–60 showed definite localisation: this finding can be matched by Eisenberg et al. (1958), who found that the infection was localised in 14% of their series of 75 hospital cases. In contrast, Seligmann et al. (1946) examined a series of 1107 cases from many sources, and noted only 51 (i.e., 5%) patients with localised infection.

Some of the reasons for this disproportion are as follows. A general hospital is usually very reluctant to admit patients who might have salmonella gastroenteritis or salmonella fever; thus a patient admitted primarily with a salmonella infection is unlikely to be a typical case. Pre-existent disease also plays a part. Saphra (1950) noted that in elderly debilitated patients resistance may be so lowered that hitherto symptomless salmonella infections may spread and invade the blood-stream; one may reasonably suggest a similar sequence in acute salmonella infections.

Several workers have noted a relationship between surgery and salmonella infections. Harvey (1937) reviewed 21 cases of sporadic *S. choleræsuis* infections, and found such an association in several of them. Three main reasons for this have been suggested by Black et al. (1960). In the first place a latent infection may be activated by the patient's altered physiology after surgery. Secondly, the surgeon may spread the infection through his handling of the gut at operation, and finally, many patients undergoing surgery are nowadays given intensive preoperative treatment with antibiotics which might suppress competition by normal gut organisms.

All the patients here described presented as cases of abdominal disease, usually with pain and pyrexia; diarrhœa was often a late symptom, and vomiting was uncommon. Although they differed from the classical pictures of salmonella infections, none of these cases is unique. Seligmann et al. (1946) recorded a splenic abscess caused by *S. choleræ-suis* which is comparable to that of case 1 in this series. Case 5 is matched by that of Roberts and Barron (1958), who point out that genital ulceration was a well-recognised complication of typhoid fever fifty years ago. The pseudosurgical syndrome produced by some salmonella infections is generally known, and appendicectomy is a not infrequent complication (Bornstein 1943). Black et al. (1960) have found much difficulty in deciding whether the syndrome represents a true bacterial involvement or merely right-iliac-fossa symptoms associated with a salmonella enteritis.

Fæcal cultures were positive in all but one of these patients; and, although the diagnosis was made by other means in five cases, there seems no doubt that fæcal culture is the most reliable method of isolation. Angrist and Mollov (1946) and Seligmann et al. (1946) also found this to be true. It is perhaps worth emphasising the possible value of fæcal culture in cases with obscure abdominal symptoms even in the absence of diarrhœa or other gastrointestinal features.


### Summary

9 cases of unusual salmonella infection were seen in a general hospital during the four-year period 1956–60.

The patients usually presented as cases of abdominal disease with pain and pyrexia, and with diarrhœa as a late symptom. Not infrequently the infection showed definite localisation.

There is a higher incidence of atypical examples of salmonellosis in hospitals. Fæcal culture seems to be the most reliable method of diagnosis.


I am very grateful to Dr. R. L. Vollum for his advice and encouragement in the preparation of this paper; and to the following clinicians for their permission to report the cases: Prof. L. J. Witts (cases 1 and 6), Prof. Chassar Moir (case 5), Mr. D. C. Corry (cases 3, 8, and 9), Mr. A. Elliot-Smith (case 4), and Mr. M. P. Embrey (case 7). Case 2 was admitted to the Radcliffe Infirmary under the care of the late Mr. D. A. Abernethy.

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# PLATELET ECONOMY DURING MODERATE AND INTENSIVE DICOUMAROL THERAPY


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DICOUMAROL in sufficient dosage has been shown to depress platelet adhesiveness and delay platelet clumping *in vitro* (Murphy and Mustard 1960), and to prolong platelet survival *in vivo* (Murphy and Mustard 1961). In the therapeutic use of dicoumarol, it has been tacitly assumed that small doses produce proportionate effects, and that if they confer little benefit at least they do no harm. There have been indications, however, that this is incorrect (Horlick 1961). Accordingly, we have studied the effects of giving dicoumarol in doses sufficient to produce smaller and larger changes in blood coagulation.

## Patients and Methods

The most efficient method of studying the effects of different levels of dosage is by comparison of the values in the same subjects under different regimens. Because the measurement of platelet-survival requires the injection of a radioactive isotope, toxicity limits the number of studies on each subject. A group of twelve patients, who had sustained complications of atherosclerosis, were studied during high dosage with dicoumarol, and later after the dose had been reduced; and the results were compared with each other and with those from a comparable untreated group of atherosclerotic patients reported elsewhere (Murphy and Mustard 1961). For the low-dosage studies our aim was to keep the prothrombin-time below 20 seconds during and for 4 days before the study. The control value in this laboratory is 11·7–15·2 seconds.

*Coagulation tests.*—The whole-blood clotting-time, the one-stage prothrombin-time, the platelet-clumping-time, the plasma-thromboplastin-time, and the platelet-adhesive-index were measured as previously described (Murphy and Mustard 1960).

*Platelet-survival and turnover* were measured by a modification of the di-isopropyl fluorophosphonate phosphorus-32 (D.F.P.$^{32}$) technique of Leeksma and Cohen (1956), and were computed as described elsewhere (Murphy and Mustard 1961). There has been much dispute whether platelets are randomly consumed, giving an exponential survival curve, or die of old age, giving a curve which follows a complex integral that we have called " gaussian ". Because there are, as yet, no clear indications as to which is correct, we have computed the results both ways.

*Statistical considerations.*—Whole-blood clotting-time and platelet-clumping-time are log-normally distributed, whereas the reciprocals of the plasma-thromboplastin-time are normally distributed. The other variables required no transformation (Murphy and Mustard 1960, 1961).

## Results

*In-vitro tests*

The low-dosage regimen produced a small average lengthening of the prothrombin-time (about 26%) and the plasma-thromboplastin-time (about 17%), but in the other tests it produced an average change, as compared with the untreated group, in the direction of increased coagulability (table I). High dosage, however, produced a mean lengthening of prothrombin-time of about 115%,

TABLE I—IN-VITRO COAGULATION TESTS

| Group | No. | Mean age (yr.) ±S.E. | Tests: Mean adhesive index | Mean platelet-clumping-time (sec.) | Mean clotting-time (min.) | Mean prothrombin-time (sec.) | Mean platelet-count (no. per c.mm.) | Plasma-thromboplastin-time (sec.) |
|---|---|---|---|---|---|---|---|---|
| Untreated (U) .. .. | 31 | 55·29 ±1·98 | 1·250 | 308 | 12·65 | 14·1 | 222,500 | 11·6 |
| Low-dosage (L) .. | 12 | 53·58 ±3·07 | 1·284 | 288 | 11·26 | 17·8 | 193,400 | 13·7 |
| High-dosage (H) .. | 12 | 53·58 ±3·07 | 0·994 | 405 | 16·79 | 31·2 | 214,300 | 19·5 |
| Significance of Differences between means (*t* values): U and L .. .. | | 0·460 | 0·630 | 1·075 | 1·797 | 5·502‡ | 3·179‡ | 3·624‡ |
| U and H .. .. | | 0·460 | 5·459‡ | 3·399† | 2·906† | 10·503‡ | 0·603 | 9·263‡ |
| L and H (paired) .. | | — | 4·167† | 4·217† | 3·073* | 6·798‡ | 1·560 | 5·583‡ |

* $P<0.05$; † $P<0.01$; ‡ $P<0.001$.

TABLE II—IN-VIVO COAGULATION TESTS

| Group | No. | Mean age | Tests | | | |
|---|---|---|---|---|---|---|
| | | | Platelet half-life exponential days | Platelet turnover exponential (no. per c.mm., per day) | Platelet half-life gaussian days | Platelet turnover gaussian (no. per c.mm. per day) |
| Untreated (U) .. .. | 31 | 55·29 ±1·98 | 2·86 | 58,220 | 10·04 | 22,870 |
| Low-dosage (L) .. | 12 | 53·58 ±3·07 | 2·60 | 54,160 | 10·06 | 19,450 |
| High-dosage (H) .. | 12 | 53·58 ±3·07 | 4·13 | 39,010 | 12·11 | 18,240 |
| Significance of differences between means ($t$ values): U and L | | 0·460 | 1·173 | 0·712 | 0·047 | 2·276* |
| U and H .. .. | | 0·460 | 3·642‡ | 3·431† | 3·992‡ | 2·136* |
| L and H (paired) .. | | — | 4·443‡ | 2·648* | 4·369‡ | 0·662 |

* $P > 0.05$; † $P < 0.01$; ‡ $P < 0.001$.

and this was associated with lengthening of clotting-time, platelet-clumping-time, and plasma-thromboplastin-time, and with a considerable decrease in the adhesive index. These differences achieve statistical significance which is perhaps in part attributable to the increased sensitivity that results from the study of paired differences.

*In-vivo tests*

These showed analogous results (table II). Low dosage shortened the mean platelet survival, calculated as an exponential, although not significantly; whereas high dosage caused considerable lengthening with a corresponding diminution in platelet turnover.

## Discussion

By comparing a treated with an untreated group, we have previously shown that dicoumarol influences platelet economy (Murphy and Mustard 1960, 1961). The present results establish this conclusion more directly in that the same group of patients were studied at two levels of anticoagulation.

That a powerful pharmacological agent like dicoumarol should have been under clinical study for some 20 years without unassailable conclusions being drawn about its efficacy is itself reason for wondering whether low dosage may be harmful. Some studies, such as that of MacMillan et al. (1960), suggest that it is deleterious. Light has been thrown on this by the studies of Horlick (1961), who showed that induction of dicoumarol therapy may be associated with a temporary increase in platelet adhesiveness; and it is a commonplace clinical observation that abrupt cessation of therapy is fraught with danger. It is desirable that more direct evidence be obtained about the effects on coagulation within the body; and, as we have pointed out elsewhere, the only suitable quantitative *in-vivo* measures of the early stages of coagulation at present available are platelet survival and turnover. The reasons for directing our attention to the early stages of coagulation and platelets, rather than to frank fibrin formation, have already been discussed (Murphy and Mustard 1960, 1961).

Ashwin (1961) has shown in rats that intravascular thrombosis in damaged vessels is, if anything, enhanced by giving dicoumarol in doses which keep the prothrombin-time less than twice normal.

More direct evidence about the effect, in pigs, of dicoumarol on thrombus formation, by using extracorporeal shunts, has been reported (Murphy, Downie, Robinson, Rowsell, and Mustard 1961). In brief, we showed that, under standardised experimental conditions, low dosage with dicoumarol led to a sixfold increase, compared with the results of experiments on control animals, in the weight of thrombus formed in a flow chamber; high dosage reduced deposit formation. These differences were independent of the rate of flow, but they correlated well with coagulant activity, notably with the platelet-adhesive-index ($r = +0{\cdot}69$, $P < 0{\cdot}001$).

Low dosage was associated with a significant depression of the platelet-count; but, as in previous studies, depression was similar in the untreated and high-dosage groups. These counts were made on venous blood, and hence we do not know how far the low counts were due to diminished production, and how far to increased destruction on the arterial side.

We now present evidence that intermediate degrees of dicoumarol dosage are *not* associated in man with intermediate effects on platelet physiology, either *in vitro* or *in vivo*. Although the evidence does not conclusively indicate a biphasic effect, it shows that under the conditions of this study the smaller doses of dicoumarol did not tend to decrease platelet adhesiveness or to lengthen platelet survival.

Horlick (1961) showed that after an acute myocardial infarction the adhesive index tends to rise spontaneously. This, added to the effects of incomplete dicoumarol therapy, may partly explain why he observed bigger changes in platelet adhesiveness with low dosage than we found in our study. In this study, as in our previous ones, no patient was included who had sustained an infarction within the previous 3 months. A further point of difference is that Horlick studied subjects in whom dicoumarol therapy had recently been started, whereas ours had had high doses for some months.

A common defect in the many reports on the treatment of coronary disease with dicoumarol is a failure to specify the precise criteria of desirable anticoagulant control. Borchgrevink's study (1960) is unique in that he attempted not merely to evaluate the efficacy of dicoumarol therapy but also to compare the effects of different levels of control. He has, in fact, shown that high dosage has a greater prophylactic effect than low dosage, but unfortunately his study does not include a completely untreated group.

McMichael and Parry (1960) attributed the discrepancies between the conclusions of the working party of the Medical Research Council (1959) and those of MacMillan et al. (1960) to the vagaries of sampling. We think it important to remember the possibility that it may equally well be due to differences in regulation of dosage. While the M.R.C. gave a therapeutic range for the prothrombin-time of 2–2$^1/_2$ times normal, MacMillan et al. aimed at a level of 20–30 seconds (i.e., 1·25–1·88 times their control value of 16 seconds). It is important for future investigators to recognise that safe and effective dosage with dicoumarol can probably be achieved only within a therapeutic range bounded above and below by danger zones.

Attaining this objective may prove in practice to be a formidable task.


### Summary

Doses of dicoumarol which appear to produce slight depression of coagulation as judged by prothrombin-time, seem to have, if anything, the opposite effect on coagulation as judged by other tests both *in vitro* and *in vivo*. High doses produce a uniform depression of all tests. These findings suggest that half-hearted treatment with dicoumarol may be worse than none.

Paired comparisons between the same group of twelve patients during moderate and intensive dicoumarol treatment confirm the conclusions from previous studies that dicoumarol influences platelet economy



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## THE MURMUR OF PULMONARY REGURGITATION WHICH IS NOT ASSOCIATED WITH PULMONARY HYPERTENSION


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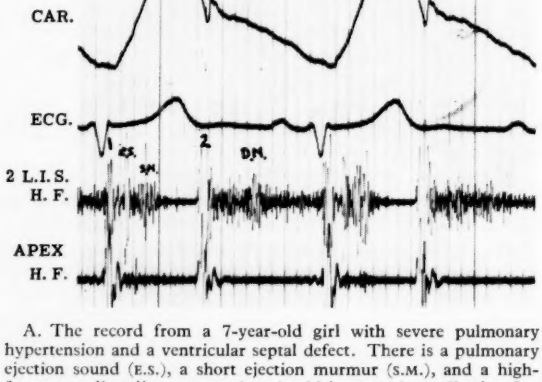
PULMONARY regurgitation most commonly results from dilatation of the valve ring secondary to severe pulmonary hypertension. The murmur of this lesion closely resembles that of aortic regurgitation and may easily be confused with it. Both are high-pitched, well heard down the left sternal edge, start almost immediately after the aortic sound, and often extend throughout diastole (fig. 1A).




A. The record from a 7-year-old girl with severe pulmonary hypertension and a ventricular septal defect. There is a pulmonary ejection sound (E.S.), a short ejection murmur (S.M.), and a high-frequency diastolic murmur (D.M.) which starts immediately after the intense fused second sound (2) and continues up to the next first sound.

PATIENTS WITH SURGICALLY PRODUCED PULMONARY INCOMPETENCE

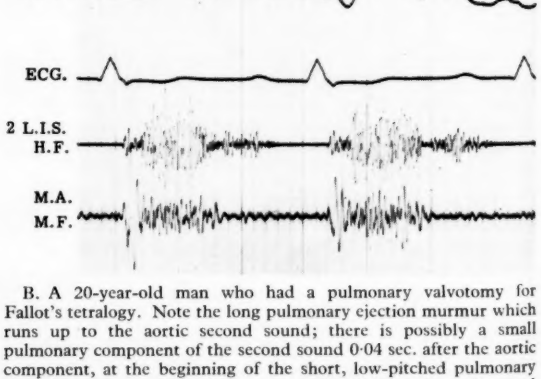
| | | |
|---|---|---|
| Pulmonary stenosis alone | | 3 |
| Valvular stenosis | 2 | |
| Infundibular stenosis | 1 | |
| Fallot's tetralogy | | 8 |
| Pulmonary valvotomy only | 2 | |
| Pulmonary valvotomy with closure of the ventricular septal defect ("total correction") | 6 | |

Where there is no hypertension, lesions of the pulmonary valve leading to regurgitation are rare. Some incompetence, however, is not uncommon after radical surgery for pulmonary stenosis. The murmur then produced differs from that of pulmonary hypertension. The purpose of this paper is to draw attention to the distinguishing features of this murmur which may now be met more frequently. Though these features have been mentioned in the literature, only a few examples of the murmur have been reported, and it does not appear to be widely known.

In a case-report, Kohout and Katz (1955) described an example but did not comment on its peculiar qualities; Hanson et al. (1958) noted its shortness but did not mention its other features. In his monograph, McKusick (1958) briefly described these characteristics; but, despite his very thorough review, he could quote only accounts by Holldach and his colleagues in the German literature, and a reference to the quality of the murmur of experimentally produced pulmonary regurgitation in dogs. In several standard cardiological textbooks (Evans 1956, Friedberg 1956, Keith et al. 1958, Kjellberg et al. 1959, Nadas 1957, Wood 1956, White 1951), and in recent reviews of phonocardiography (Castle and Craige 1960, Grishman et al. 1960, Leatham 1958) this murmur is not mentioned.

### Material

13 patients with pulmonary regurgitation have been studied. None had severe pulmonary hypertension. In 11 the lesion followed surgical relief of pulmonary stenosis (see table); but in the other 2 it was not due to surgery. Of these, one had an aortic-pulmonary septal window; after repair of the defect pulmonary regurgitation persisted though the pulmonary pressure had fallen. The other patient had a ventricular septal defect with pulmonary infundibular stenosis and atresia of the left pulmonary artery; the mechanism of the regurgitation was not clear in this patient and it may have been from the




B. A 20-year-old man who had a pulmonary valvotomy for Fallot's tetralogy. Note the long pulmonary ejection murmur which runs up to the aortic second sound; there is possibly a small pulmonary component of the second sound 0·04 sec. after the aortic component, at the beginning of the short, low-pitched pulmonary diastolic murmur, which has a crescendo-diminuendo outline and finishes just after the P wave of the electrocardiogram at the time the atrial *a* wave rises (not shown in this record).

**Fig. 1—Phonocardiograms showing the differences in timing, duration, and outline of the pulmonary diastolic murmur with pulmonary hypertension (A) and without it (B).**

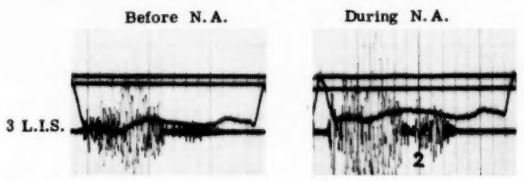



**Fig. 2—Phonocardiograms recorded at the time of cardiac catheterisation, before and during the administration of noradrenaline.**

The patient, who had had a pulmonary valvotomy for Fallot's tetralogy, is the same as in fig. 1B. Noradrenaline accentuates the pulmonary component of the second sound (2) so that it is clearly identifiable and both intensifies and shortens the pulmonary diastolic murmur.

infundibular chamber into the main cavity of the ventricle, as described by Bevegård et al. (1959).

All the murmurs were originally detected and their quality studied by the usual clinical methods of auscultation. Phonocardiograms were recorded (on the multichannel photographic equipment manufactured by New Electronic Products, Ltd.), and in 5 patients the effect of noradrenaline administration on the record was studied.

## The Murmur

*Duration.*—The murmur was short in all the patients. In the 12 with pulmonary stenosis it started 0·02–0·08 sec. after the aortic second sound; this delayed onset probably corresponded to the pulmonary second sound which could not,

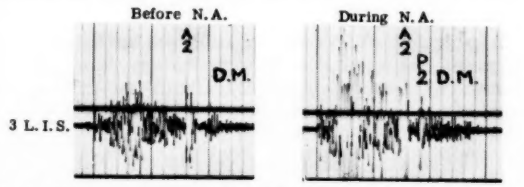



**Fig. 3—Phonocardiograms recorded, during cardiac catheterisation, before and during the administration of noradrenaline.**

The patient was a 10-year-old boy who had had an isolated infundibular stenosis resected. Note how the pulmonary component of the second sound (P2), previously difficult to distinguish from the beginning of the pulmonary diastolic murmur (D.M.), becomes accentuated and clearly identifiable after noradrenaline. A2: aortic component of second sound.

however, be clearly heard or recorded. It usually stopped in mid-diastole, commonly at the time of the upstroke of the atrial *a* wave, when the pressure gradient between the pulmonary artery and right ventricle was probably abolished. The 13th patient, with the aortic-pulmonary window, had a loud fused second sound before operation but afterwards normal splitting was heard on inspiration; the murmur then began after the pulmonary component.

*Configuration.*—The amplitude rose to a crescendo, as a result of the initially increasing pulmonary artery/right ventricular gradient in early diastole, and then fell till the murmur ended in mid-diastole. Fig. 1 illustrates the differences in timing, duration, and outline of the pulmonary diastolic murmurs in the presence and absence of pulmonary hypertension.

*Site.*—The murmur was loudest in the second or third left interspace. When sufficiently loud it was transmitted down to the lower left sternal border, where it somewhat resembled the murmur produced, for example, in atrial septal defect by increased flow through the tricuspid valve (so-called " flow " murmur).

*Pitch.*—The low pitch of the murmur could be readily appreciated, and contrasted strikingly with the high pitch of the murmur of pulmonary regurgitation secondary to pulmonary hypertension.

*Effect of Giving Noradrenaline*

To both the patients with Fallot's tetralogy in whom the ventricular septum was still patent, noradrenaline was given by infusion (10–20 μg. per min.) during cardiac catheterisation. 1 had only mild pulmonary hypertension before the pressor agent was administered, the other none. To 3 other patients (2 with isolated pulmonary stenosis and the 1 with uncorrected Fallot's tetralogy and atresia of a pulmonary artery) the noradrenaline was infused by slow intravenous injection (20–40 μg.).

The diastolic murmur was accentuated in all the patients; and the murmur became obvious in the 3 in whom it was ordinarily soft. In the 2 with Fallot's tetralogy not completely corrected, the wide communication between the two ventricles coupled with the increase of systemic resistance resulted in a

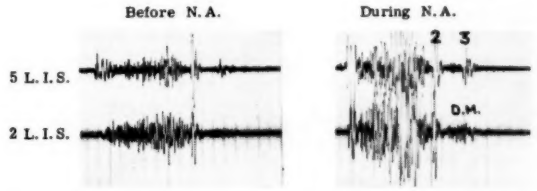



**Fig. 4—Phonocardiograms recorded before and during the administration of noradrenaline.**

The patient was a girl of 17 who had had a valvotomy for isolated pulmonary stenosis. The noradrenaline has intensified all the recorded phenomena; the soft pulmonary diastolic murmur (D.M.), in particular, is better defined. 2: aortic second sound. 3: third heart sound.

considerable rise of the end-diastolic pressure in the right ventricle. Consequently right ventricular and pulmonary arterial diastolic pressures became equal earlier, and the murmur became shorter (fig. 2).

The pulmonary component of the second sound was intensified and became clear after giving noradrenaline to 2 patients (figs. 2 and 3). In another patient a third heart sound, probably of right ventricular origin, as well as the pulmonary diastolic murmur, was intensified with noradrenaline; both these sounds were ordinarily soft and hard to distinguish (fig. 4).

## Discussion

Though the pulmonary valve lesions were the result of surgery in nearly all our patients, we think that the murmur we describe is characteristic of all pulmonary

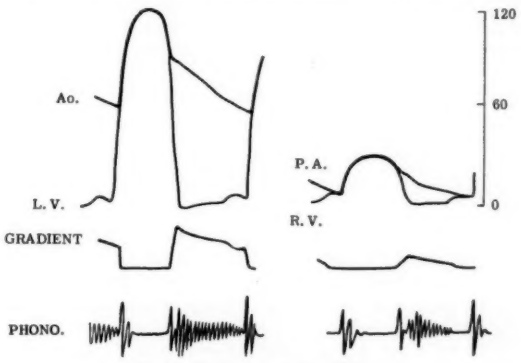



**Fig. 5—Pressure relationships.**

The diagram on the left indicates (above) the pressure relationships between the aorta and left ventricle (or pulmonary artery and right ventricle when severely hypertensive) in the presence of valvular incompetence; the gradient between them is shown below the pressure curves (not to scale). On the right pulmonary regurgitation without hypertension is illustrated. Note that the diastolic gradient is much less in this case, and that it is abolished before the end of diastole, in part by the upstroke of the atrial *a* wave. The corresponding form of the diastolic murmurs is shown at the bottom.

regurgitation which is not secondary to pulmonary hypertension. This is supported by the presence of a similar murmur in the 2 patients who had not had operations on the valve. The hæmodynamics which apparently determine the characteristics of the murmur are the same irrespective of the cause of the incompetence (fig. 5).

The low pitch is probably the most characteristic feature of the murmur, since occasionally an aortic diastolic murmur may seem delayed, since its initial vibrations are inaudible (Leatham 1949). The term "rough" describes the murmur quite well (Kohout and Katz 1955): this roughness may help to differentiate it from a "flow" murmur. It seems reasonable to suppose that the low pitch of the murmur is related to the small diastolic gradient between the artery and ventricle when there are organic lesions of the pulmonary valve (fig. 5). One of our most instructive patients was the boy whose aortic-pulmonary window had been successfully closed. Before this his aortic and pulmonary arterial pressures had been equal and a typical high-pitched, long, pulmonary diastolic murmur had been present. After the repair the pulmonary arterial pressure, measured at operation, fell immediately; and postoperatively the pulmonary regurgitant murmur was low-pitched and short.

The crescendo-diminuendo configuration of the murmurs is often striking. The crescendo is probably more obvious because the murmur starts after the soft pulmonary component of the second sound and so is usually well separated from the louder aortic component. Aortic diastolic murmurs have the same pattern (Wells et al. 1949) but it is usually not so obvious (McKusick 1958).

Sometimes the recognition of the murmur may not be merely of academic interest:

A boy of 15 (not included in our series) had an operation for total correction of Fallot's tetralogy. Benefit was considerable at first, but soon after operation a high-pitched regurgitant murmur was heard, which was thought to be pulmonary in origin. This was held to account for an increased right ventricular heave which developed shortly afterwards. The boy's condition deteriorated rapidly and the systemic pulse pressures increased, suggesting an aortic leak. Further surgical exploration was unsuccessful. Necropsy showed that a suture used to close the ventricular septal defect had perforated the base of an aortic cusp; and the right ventricular heave was due to an aneurysm at the ventriculotomy site. Earlier recognition that the diastolic murmur was not like that of surgically produced pulmonary regurgitation might have led to an earlier, and possibly successful, re-exploration to correct the aortic lesion; examples of this have recently been reported (Fell 1960).

**Summary**

The murmur which pulmonary regurgitation causes when the pulmonary arterial pressure is normal or only slightly raised (most commonly a sequel to surgical correction of pulmonary stenosis) differs from the murmur it causes when the pressure is high. It is characteristically low-pitched and short, and usually has a well-marked crescendo-diminuendo configuration. If faint, it can be recognised and recorded more easily after giving noradrenaline.

This work was done while one of us (G. A. B.) was holding a scholarship from the S. Achillopoulos legacy, Volos, Greece, which is gratefully acknowledged. We are also indebted to Dr. Charles Baker and Sir Russell Brock for allowing us to study and report on their patients.

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*References continued at foot of next column*

## Preliminary Communication

# OBSTETRIC ANALGESIA

## The Use of a Fixed Nitrous Oxide and Oxygen Mixture from One Cylinder

THIS communication is intended to publicise the fact that clinically useful mixtures of nitrous oxide and oxygen exist as a single gas phase at 2000 pounds per square inch on the gauge (P.S.I.G.) In the past theoretical considerations seem to have discouraged research into this possibility.

The use of gas mixtures from one cylinder is not new: in 1945 Barach and Rovenstine [1] recommended an 80% nitrous oxide and 20% oxygen v/v mixture, at a maximum cylinder pressure of 700 lb., for use in nitrous-oxide anæsthesia. Recently Dr. J. W. Haworth, of the British Oxygen Company Ltd., has shown that, at a pressure of 2000 P.S.I.G., oxygen has a considerable solvent effect on liquid nitrous oxide; and at this pressure, at room temperature, 75% nitrous oxide and 25% oxygen v/v exists as a single gas phase in the cylinder. This applies to all proportions of nitrous oxide in oxygen up to 75% v/v, but not above. The solvent action of compressed gases is known as the Poynting effect.

At St. Mary's Hospital, Portsmouth, a mixture of 50% nitrous oxide and 50% oxygen v/v, contained in one cylinder, has been used for the relief of pain in childbirth with the same effect as a corresponding mixture of gases from separate cylinders.

A great deal of development work will have to be done to assess the merits of this method of administering nitrous oxide and oxygen, and this will take time. Mixtures of nitrous oxide and oxygen in one cylinder are not generally available, and they have to be specially prepared in the laboratory. All the physical limits of such mixtures are not yet fully defined, and the mixtures are very much in the experimental stage. However, the discovery that nitrous oxide, up to 75%, in oxygen remains in the gas phase until well above the pressure at which it normally becomes a liquid, holds promise for two reasons. Firstly, the cylinder space is utilised to the full; and, secondly, the nitrous oxide used for analgesia is made inseparable from a safe proportion of oxygen by a process which depends neither on a mixing device nor on two cylinders with different rates of emptying.

I wish to thank the British Oxygen Company Ltd. for their vital help in research, supplying equipment, and providing the gases. I should also like to thank Dr. R. J. Hamer Hodges for his ever present help and encouragement.

St. Mary's Hospital, Portsmouth, Hants.

M. E. TUNSTALL
M.B. Lond., F.F.A. R.C.S., D.OBST.

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# Reviews of Books

## The Scientific Basis of Medicine

*Annual Reviews* 1961. University of London: The Athlone Press. 1961. Pp. 342. 40*s*.

THE theoretical basis of the doctor's work undergoes continual revision, and the most recently published lectures given under the auspices of the British Postgraduate Medical Federation recognise this fact in the new title. The lectures deal mainly with the laboratory approach, presenting rounded and readable digests of new knowledge by experts: problems of genetic analysis (Pontecorvo) and cellular immunology (White); the epidemiological approach to leukæmia (Doll); blood enzymes in diagnosis (Wilkinson); and biochemical studies of aminoacid metabolism (Dalgleish and Milne). There are essays on the non-pancreatic types of diabetes mellitus (Gray) and also liver failure (Sherlock) which indicate a complete revolution in approach and outlook. Plasma lipids (James), magnesium deficiency (Fourman), and multiple sclerosis (Thompson) are further topics of general interest, while the lecture on the effects of some drugs on the heart (Vaughan Williams) should open the minds of specialist cardiologists to new possibilities. The index includes the titles dealt with in the previous eight volumes and a cumulative index is promised in the future development of this series. This volume is not entirely filled with strenuous scientific endeavour for it begins and ends with philosophical discourses by Sir Lindor Brown and Sir Roy Cameron, the latter giving a thrilling account of his own evolution as a leader in the field of experimental pathology.

These attractive records of contributions to basic medical science in this country deserve continuing success.

## A Study of the Psychiatric Nurse

AUDREY L. JOHN, B.COM., PH.D., S.R.N., S.C.M., research fellow, Nursing Studies Unit, University of Edinburgh. Edinburgh: E. & S. Livingstone. 1961. Pp. 239. 21*s*.

THIS first publication from the Nursing Studies Unit of Edinburgh University examines some aspects of mental nursing in Britain today. The author, a general-trained nurse and a university graduate, spent three years observing and analysing nursing work in four mental hospitals; and she was awarded a PH.D. for this study, which is here clearly and attractively recorded. Though Dr. John calls them " British hospitals " there is internal evidence that they are all in Scotland.

She collected her information by taking part in the work in the wards, by questionaries, from diaries kept by student nurses, and by interviews of a random sample of all grades of nursing staff. She describes the type of work and the physical working conditions; the types of patients and the way in which the wards work; the different grades of nurses and their relationships with one another and with the doctors. She finally discusses communications, recruitment, health, and morale. She shows that the nursing in these hospitals was poor: " it is a harsh picture of technical inefficiency—stemming from confusion of jobs and low morale, and intimately related to poor staff relations and communications ". She points to the need for improved conditions of work (such as the abolition of ancient insanitary sluice rooms), for better methods of selection of nurses, and for better communications (" nurses had little or no access to case notes and were frequently not even told of changes of policy in relation to patient care "); but, she feels, the great need is to clarify the roles of the " nurses ". She recommends that assistant nurses, at present called " nurse " (but often quite untrained), should be separated and given some training, possibly like the State-enrolled assistant nurse; and those unable to undertake this training should be regarded as ward orderlies. For the student nurses she advocates a comprehensive basic training with general nursing.

This valuable book gives a clear picture of the low standard of nursing in certain hospitals in 1957–60. But it would be a pity if it were taken as representative of all British psychiatric nursing today. There are many hospitals where things are much better, and it is perhaps there that answers to these problems should be sought. In many psychiatric hospitals nursing assistants are trained, the nurses do have access to case-notes, and regular staff conferences ensure that the nurses are informed of policy changes. The General Nursing Council experimental syllabus (not in use in these four hospitals) offers a good psychiatric nursing training which many believe to be better than any comprehensive scheme.

## The Serology of Conglutination and its Relation to Disease

R. R. A. COOMBS, M.R.C.V.S., B.SC., PH.D., ANNE M. COOMBS, B.A., PH.D., D. G. INGRAM, D.V.M., M.V.SC., PH.D. Oxford: Blackwell Scientific Publications. 1961. Pp. 210. 40*s*.

IN 1902 Paul Ehrlich and Hans Sachs reported an observation in support of Ehrlich's theory that complement combined chemically with the antibody rather than, as Bordet thought, by physical adsorption. Ehrlich envisaged a reaction between complement and antibody before the antibody had combined with the antigen on the cells, and Bordet considered that the physical adsorption of complement could only occur after antibody and red cells had combined. The experiment of Ehrlich and Sachs consisted in adding fresh horse serum to guineapig red cells, when hæmolysis took place in the presence of heated bovine serum; but if after exposure to the heated bovine serum, the cells were washed before adding the fresh horse serum, hæmolysis did not occur. Ehrlich considered this as proof that previous absorption of heated bovine serum with guineapig cells did not prevent hæmolysis and hence the antibody did not combine with cells unless it had previously been united with complement.

The name of conglutination has unfortunately been given to another and quite distinct serological reaction by Wiener 43 years later, and the authors of this book plead strongly that the confusion of terminology should now be allowed to die out. This book gives a historical survey of work on conglutination and describes the studies of Dr. Coombs and his team in this subject. In animals a conglutinin-like substance can be produced by the injection of absorbed complement. Furthermore, conglutination has been shown to appear in the blood of men and animals during infective diseases. There is some evidence that this phenomenon is one of the factors concerned in " non-specific resistance ".

The authors also consider that the immunoconglutination which arises during a natural infection seems to fulfil the criteria laid down for an autoantibody formed against the body's own complement. Thus autoantibody formation under natural conditions may, in the case of immunoconglutinin production, be actually beneficial.

This well-written book can be recommended to all who want to keep themselves informed on this fascinating aspect of immunology.

## Tobacco: Experimental and Clinical Studies

*A Comprehensive Account of the World Literature*. P. S. LARSON, PH.D., professor of pharmacology, H. B. HAAG, M.D., professor of pharmacology, H. SILVETTE, PH.D., visiting professor of pharmacology, Medical College of Virginia, Richmond, Virginia. London: Baillière, Tindall & Cox. 1961. Pp. 932. 160*s*.

THIS astonishing labour is justly dedicated to the authors' wives' " incredible patience ", for it contains a survey of over 6000 articles from 1200 journals on topics ranging from a case-report of 1848 describing the use of a tobacco enema in effecting a complete cure of " a permanent contraction of the muscles originating on the right side of the pelvis " to a detailed survey of the question of smoking and lung cancer. Some may wonder whether such huge compilations of " good work and bad, sound and uninformed opinion " serve any useful purpose beyond that supplied by a simple bibliography. Sometimes the authors act the part of informed guides, but not always. It may well be that the future of such books, designed to cover the whole of the past of a subject, will rather lie in the critical review supplemented by a full and classified bibliography.

Whatever the answer, there is no disputing that anyone

interested in any aspect of tobacco will find his knowledge extended if he consults this compendium, which has been partly supported by the Tobacco Industry Research Committee.

### Darwinism and the Study of Society

*A Centenary Symposium.* Editor: MICHAEL BANTON. London: Tavistock Publications. 1961. Pp. 191. 21*s*.

FOR a hundred years an influential school of thought has maintained that heredity, in its interaction with other factors, determines the major features of social life. In 1959 the centenary of *The Origin of Species* was celebrated by a conference whose object was to reassess the relevance of biological principles to social studies. Essays based on papers read at the conference have been gathered into a book, to which Dr. J. Bronowski has written an introduction.

Contributors include Basil Willey on Darwin's Place in the History of Thought, Lancelot Hogben on Darwinism and Human Society in Retrospect, C. H. Waddington on The Human Evolutionary System, and S. A. Barnett on Communication in Animal and Human Societies. Sociological contributions include Morris Ginsberg on the Social Evolution, Tom Burns on Social Norms and Social Evolution, and W. Stark on Natural and Social Selection. Topics discussed include the social value of the survival of the fittest (" the survivors can at least use it as proof of their own fitness ", says Bronowski); the nature of normality; the development of religion; and the nature of communication. Summing up the book, the editor believes that sociological problems are independent of biological problems, and therefore need to be pursued separately. Nevertheless sociologists and biologists have much to learn from one another, and this book will play its part in improving communication between them.

### The Newborn Child

DAVID G. VULLIAMY, M.D., M.R.C.P., D.C.H., consultant pædiatrician, West Dorset and South Somerset Group of Hospitals. London: J. & A. Churchill. 1961. Pp. 163. 15*s*.

THIS handy little book is a clear and accurate outline of contemporary thought and practice in this important subject. There are 34 good illustrations, and it will be particularly useful for medical students and nurses who are looking for the essential facts about the care and minor disturbances of the newborn in easily accessible form. There are no references, but the well-chosen suggestions for further reading will prove very useful in a book of this kind.

### Foundations of Psychopathology

JOHN C. NEMIAH, M.D., associate in psychiatry, Harvard Medical School, and psychiatrist, Massachusetts General Hospital. New York and London: Oxford University Press. 1961. Pp. 338. 52*s*.

BASED on the author's lectures to second-year Harvard medical students, this book gives an outline of analytically oriented theories on psychopathology applied to clinical practice. It suffers from its loose systematic structure and from a discursiveness in the many case-histories which illustrate its teachings. Much sound sense and clinical insight is thus not so apparent as it might be. The judicious skipper, however, will find the sections on symptom formation and on emotions, illness, and the therapeutic relationship informative and stimulating.

### Inflammation and Diseases of Connective Tissue

(*A Hahnemann Symposium.* Philadelphia and London: W. B. Saunders. 1961. Pp. 900. 112*s*.)—The usefulness of a symposium, it is widely held, lies at least as much in the discussions as in the papers. Inclusion of both in a published version, therefore, aims to revivify and disseminate more widely the ideas and opinions generated by the symposium itself. This method of reporting seems to do best when the number of contributors is small and their interests are varied. Larger meetings often seem less fertile. This symposium in Philadelphia in December, 1960, was a large one, with 148 contributors, nearly all American, and this account has been notably successful in overcoming the difficulties arising from size. Its editors, Dr. Lewis C. Mills and Prof. John H. Moyer, have skilfully fashioned their many tape-recordings into concise disquisitions usefully linking the wide range of topics—basic aspects of connective tissue, healthy and diseased, the pharmacology and metabolic activity of steroids, and the use of steroids and other anti-inflammatory agents in treatment. The book appeared less than nine months after the symposium took place, and is thus an up-to-date cross-section of the work and views of many leading American workers. Immunological investigations account for much of the research centring on rheumatoid arthritis and systemic lupus. There are signs too of the beginning of a closer association between immunological and biochemical inquiry which holds much promise. More than half the book deals with recent experimental and clinical work on steroids, including much new material not readily to be found elsewhere. The index is not very complete, but among the book's best features are the full references at the end of many of the communications.

## New Inventions

### A TRAINING DEVICE FOR EXTRACORPOREAL CIRCULATION

DURING perfusion the heart-lung machine requires little adjustment, and control is usually simple. But practice is needed if one is to gain confidence in starting and stopping perfusion, and dealing with emergencies. For 4 years we have used an " artificial patient " for training and instruction (see figure). It consists of a vertical glass cylinder (4–5 ft. long, and 3–4 in. in diameter) nearly filled with water. A bung inserted into the base carries three tubes: one represents the arterial line, and carries water from the pump of the heart-lung machine; the second represents the venous return line, and returns water to the machine; and the third runs to a drain, allowing the " patient " to be bled from time to time.

To begin with the pump is switched off, and the venous return and " bleeding " lines are clamped. To simulate the beginning of perfusion the pump is started, and flow is increased to 3–4 litres per minute. The level of water is kept constant by opening the venous return line at a rate that matches outflow from the cylinder with pumped inflow. To simulate the end of perfusion the procedure is reversed.

A person who is trained to maintain a constant fluid level in the cylinder while flow begins, rises to 3–4 litres per minute, and falls to zero, has little difficulty in maintaining constant venous pressure and the patient's blood-volume during clinical perfusion.

Rise of venous pressure from an obstructed return line, and fall from hæmorrhage, may be simulated in the artificial patient by clamping or unclamping the appropriate line to test the trainee's alertness and speed of reaction.

The General Infirmary, Leeds, 1

P. G. F. NIXON, M.B. Durh., M.R.C.P.

THE LANCET

LONDON 28 OCTOBER 1961

## Doctor and Architect

ARCHITECTS, who in the Middle Ages looked to monks, in the counter-reformation to Prince Bishops, and in the 18th century to aristocratic landowners, may soon rely on the National Health Service for a sizeable part of their livelihood. If architects are to design hospitals effectively, they must have the informed cooperation of those—notably the doctors—who are to work in them. Now that a large programme of hospital construction is at last to be undertaken, those engaged in hospital practice will increasingly be asked to help in this way. How well equipped is the doctor to undertake such a task on the public's behalf?

Architects, asked to arrange the following in order of preference—publican, actress, business-man, manufacturer, doctor, or don—are likely to place the doctor at the bottom of the list. Some of the reasons seem clear. We have had little opportunity to think constructively about the buildings we work in; for as regards our workplaces we have lived from hand to mouth. Hospitals have been extended piecemeal as benefactions have provided money for a bed here or a ward there. Moreover, few of us are used to starting from first principles. Whereas the architect thinks from the general to the particular, the doctor usually thinks from the particular to the general. We are trained to look at things that have gone wrong and decide how to put them right; and thus when it comes to planning a building we are sometimes guilty of asking the architect to draw plans and offering to " correct " these when he returns with them. This is not the way to produce good buildings. The Festival Hall, the United Nations building, and the new Swindon Hospital were not planned in this way. They were constructed after long and painstaking analysis of the activities that were to be pursued within their walls: they are good buildings because they have been carefully devised for their differing functions. LE CORBUSIER once termed a house a *machine à habiter*. This may seem a harsh definition of a piece of architecture, and it certainly does not apply to some buildings—for instance, Blenheim Palace. But Blenheim Palace is a prestige building erected to commemorate a national victory, while a hospital (like a factory) must be designed as a whole to enable many different activities to be carried on with the greatest possible efficiency, convenience, and economy. Here the validity of LE CORBUSIER's dictum is beyond dispute.

The planning of a hospital for the National Health Service is a complex operation. Whether it is to be constructed at all will depend, first, on the total sum allotted from the Exchequer for capital development, and secondly on the strength of the claim in relation to those from other parts of the country and even of the same region. Moreover, before any final decision is reached, the planners must assure themselves that adaptation or extension of existing buildings will not provide a cheaper and equally effective alternative; and they must peer as best they can into the future in an effort to forecast shifts in population, and medical developments which may affect the demands on the various departments. The decision to build having been reached, they must review the amount to be devoted to the new building in the light of the saving that results from wise investment in, for example, mechanisation. In a modern hospital salaries and wages account for some 75% of running costs; and extra initial outlay to save labour may soon be redeemed. Furthermore, the far-from-simple technical requirements of the various departments—wards, operating-theatres, laboratories, and so on—must be met, and communication between the departments must be so devised that if possible no-one walks ten yards when he might walk five, and that the unlucky ones who must walk fifty shall be as few as possible. All this calls for precise information on functions, on volumes of work, and on the amount and direction of traffic in the building. Finally, when the plans are completed, the placing of the contracts has to be carefully timed. The building industry is relatively inelastic: it is geographically tied, and rapid expansion is difficult; and a sudden outburst of construction in one area can add remarkably to the cost.

In this difficult operation, doctors who are to work in new hospitals can help in two ways. First, they can get together and formulate their programme of medical requirements *as a team*, instead of as a series of individuals. Their programme should comprise a concise but detailed account of the procedures that they intend to carry out; the space, the staff, and the equipment that will be needed; guidance on the relation of departments one to another; and perhaps some indication of the departments which in the future may have to be expanded and of others that it may be possible to curtail. Secondly, the medical team can help by consulting an architect from the start, so that its programme is formulated in terms which are technically feasible. If this collaboration is to be fruitful, the medical side should know something of the possibilities and the difficulties of architecture; and a short series of articles, of which the first appears this week, has been written with a view to meeting this need.

## Ultrasonics as an Aid to Diagnosis

ULTRASONIC echo-sounding has been established for several years in the non-destructive testing of metals. The application of this principle to medical diagnosis is now being developed in various centres—particularly in this country,[1–3] the United States,[4 5]

1. Donald, I., MacVicar, J., Brown, T. G. *Lancet*, 1958, i, 1188.
2. Gordon, D. *Brit. med. J.* 1959, i, 1501.
3. Jefferson, A. *J. Neurol. Psychiat.* 1959, **22**, 83.
4. French, L. A., Wild, J. J., Neal, D. *Cancer*, 1951, **4**, 342. *J. Neurosurg.* 1951, **8**, 198.
5. Howry, D. H. Institute of Radio Engineers Convention Record of 1955. National Convention pt. 75–88.

Scandinavia,[6] Germany,[7] Japan,[8] and the U.S.S.R.[9]

Unlike the ionising radiations employed in radiographic techniques, ultrasonic energy consists of mechanical vibrations of a frequency far above the range of animal hearing. Every time a beam of this energy crosses the boundary, or interface, between two structures or tissues of different density, some of the energy is reflected and can be picked up and amplified as an electrical signal from a piezoelectric crystal. The depth and position of these reflecting interfaces can be plotted, as in charting the bed of the ocean; and the strength of the reflected echo, which is a measure of the difference in tissue density at the interface, provides scope for diagnosis.

Whereas sound metal is homogeneous, and the demonstration of flaws in it is relatively simple, the body has a bewildering number of tissue-planes and interfaces—to say nothing of differing absorption characteristics in each tissue traversed. Since the laws governing the angles of incidence and reflection apply to ultrasound as well as to light, a great deal of available echo information may fail to return to a detecting probe unless steps are taken to direct the beam so that it impinges at right-angles on the interface that is being studied. To overcome this difficulty, a compound multiple-angle search technique is used in Glasgow by DONALD et al.,[1] who have elaborated a type of plan-position-indicator sector scanning already used in radar. By this means two-dimensional pictures, or echograms, can provide cross-sectional views of the body in either transverse or longitudinal section. This technique has now been extensively applied in both gynæcology and obstetrics in Glasgow.[10] The work is emerging from the experimental stage as increasing experience is gained with different sorts of abdominal tumour, and already certain facts seem to be clearly established. Firstly, bowel is largely impenetrable because it always contains gas, which, by reason of its great difference in density from surrounding tissue, causes almost total reflection. Secondly, fluid is fully transonic, and whether it is enclosed and encysted or is free, as in ascites, is easily determined. Between these two extremes are all manner of differences in tissue density. In radiography the higher the frequency the greater the tissue penetration. In ultrasonics the reverse is true; and the Glasgow team have noticed that a myoma of uterus, for example, may be poorly transonic at a standard frequency of $2^1/_2$ megacycles per second, but that if the frequency is dropped to $1^1/_2$ megacycles echoes can be received from the deeper surfaces of a quite large tumour. This type of observation, extended to other types of tissue, may help to provide information besides that on contour, location, and shape. Gross obesity is no bar to ultrasonic scanning of the abdomen since fat is easily traversed, and can in fact be measured. The grossly protuberant abdomen often causes diagnostic difficulty which is not overcome by standard radiography. Apparently ultrasonography shows very significant differences between gross ascites, ovarian carcinomatosis, massive cysts, spleens, and tumours complicating pregnancy—to mention only a few of the commoner causes.

Pregnancy conditions can also be studied by this means. The fœtal head can be readily localised because the bones of the fœtal skull reflect well. As a byproduct of their research the Glasgow team are seeking to measure the biparietal diameter of the fœtal head in utero, and they regard a discrepancy of more than 2 mm. between this measurement and caliper measurement after birth as "a bad result." Fœtal echoes can evidently be obtained in early pregnancy many weeks before the fœtal skeleton is visible on radiography. By this technique it may prove possible to exclude or diagnose hydatidiform mole. Placental localisation and the very early diagnosis of twin pregnancy may be feasible only with further technical refinements.

Less sophisticated techniques, involving single-dimension probing systems, can be applied to such purposes as locating the lower pole of the kidney on deep inspiration before undertaking renal biopsy,[11] measuring alterations in anteroposterior dimensions of the heart in conjunction with electrocardiography,[7] estimating the quantity of urine in the bladder without resort to catheterisation, and detecting the shift in the position of midline structures of the brain[12] resulting from cerebral neoplasm or injury or intracranial bleeding.[6]

Ultrasonic echo-sounding by the direct contact probe method used in Glasgow has the advantage of causing the patient no inconvenience or discomfort, and can be carried out without moving the patient from bed. Any additional diagnostic aid which does not add to the patient's discomforts or hazards should be exploited; and one day every major radiological department may find that it needs to provide this ancillary service.

## Wealth and Health

As Minister of Health, Mr. ENOCH POWELL is doing something new and valuable. His addresses show a serious attempt to get below the surface of medical politics and to explain what underlies the policies and administrative decisions. So that these commentaries on the National Health Service may be as widely read as possible, they ought to be collected and republished together—including the Lloyd Roberts lecture given at the Royal Society of Medicine last week.

Speaking on Health and Wealth, Mr. POWELL began by examining the limits within which "health services pay"—within which expenditure on health increases the amount a nation produces (its "gross domestic product"). That there must be such limits is obvious: if a nation decided to allot half its resources to medical care, nobody would expect that this would lead to its producing more of other goods and services. In theory,

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11. Berlyne, G. M. *Lancet*, Sept. 30, 1961, p. 750.
12. Taylor, J. C., Newell, J. A., Karvounis, P. *ibid.* 1961, i, 1197.

of course, some nightmare dictatorship, intent on material gain, might reserve medical care for people who were economically worth preserving; but a service of this kind, treating men as economic chattels, would bear no resemblance to any known health service anywhere. In theory, again, it would be possible to concentrate expenditure on those parts of a health service which seem to produce a net return—say on immunisation or on certain types of treatment or certain types of patients. " But in real life these economically justifiable elements of a health service . . . cannot be increased without a corresponding or more than corresponding increase in the rest." Hence to say that, because 250 million working days are lost by sickness in this country, we " ought " to spend more on the N.H.S. is a fallacy: for, even if £*x* million used for medical care of workers could save more than £*x* million now lost through sickness, there is no way of ensuring that it will in fact be used for that purpose. If an additional £*x* million is given to the N.H.S., only a fraction of it will go to preventing loss of work. Thus, though some elements of outlay on health services are economically justifiable or at least self-financing, these cannot be disentangled from the rest; and (said the MINISTER) " we do not choose the next things we will do, in medicine or in the National Health Service, by any consideration of relative economic benefit". Indeed, as medical science progresses and outlay on medical services grows larger, the outlay is likely to become more and more uneconomic; for " on many fronts the progress of medical science consists not in doing things more simply and cheaply than before but in discovering more complex and difficult things to do which previously could not be done at all ". The assumption of the Beveridge report that development of the health service would reduce the number of cases requiring that service was therefore entirely unsound: and when, in 1956, the Guillebaud Committee described the N.H.S. as " a wealth-producing as well as a health-producing service " they were perpetuating the same fallacy. The truth is that

". . . it is not the health services which produce wealth, but wealth which makes possible expenditure upon the health services, like all those other expenditures of which neither the purpose nor the outcome is economic benefit but which are the specific mark of a human society and in their elaboration and refinement distinguish a civilised nation from an uncivilised, an advanced culture from a backward one ".

Since economic criteria will not serve, can some normal or right ratio between wealth and health be established empirically? As long ago as 1954, the Royal College of Physicians of London [1] put forward the suggestion that Governments should regularly provide the N.H.S. with a fixed proportion of the national income; and the same suggestion has an important place in the plans for reforming the service which Dr. JOHN SEALE is proposing.[2] But the MINISTER, who referred to the studies of SEALE and LEES (see page 977) clearly felt that the proportion of national income that should be spent on health must vary not only in different countries but at different times. After explaining the difficulty of comparing expenditure in Britain with expenditure in other countries, and the impossibility of comparing " value for money ", he did go so far as to say, very tentatively, that if Britain is spending 4–5% of her gross national product on medical care, the corresponding figure for the United States may be 5–6%. But supposing there were a " right " percentage at any moment, why should it be the same (he asked) here and in the U.S.A.; why should it be the same now as twenty years ago or twenty years hence; and why should it rise or fall at any particular rate? The amount of expenditure, he holds, is and must be arbitrary. " There never was a moment when anyone in Britain sat down, or could sit down, and determine in advance the quantum of public expenditure on health services." The bill in 1950–51, for instance, " was what got itself spent by the pre-existing services that had been taken over ", and the bill ten years later was its direct lineal descendant—the one being derived from the other by a process of additions and subtractions.

" The true picture is thus of a mass of different expenditures which grow, or are allowed to grow, subject to a compression exercised, not always very precisely or consciously, by other demands upon public expenditure and upon the national income . . . After the event, the resultant expenditures may be expressed as percentages of the gross national product for the relevant year. Indeed, it is possible to express future intended limits on expenditure as percentages of forecast future gross national product. But in practice the amount and the limitation are not derived from these calculations: they are determined by much more complex, less conscious, and in part actually unascertainable forces and pressures, which produce from year to year a certain alteration in the size and pattern of the component parts and of the whole."

To the planner, Mr. POWELL admitted, all this might seem a conclusion of despair: " not even a conscious arbitrary decision: only a bundle of public expenditures moulded from year to year by a variety of limitations partly conscious, partly automatic." But it need be depressing, he felt, only if we think in terms of money and percentages of national income and forget the realities which such figures very partially and incompletely express. " To attempt to measure the vitality and value of a service by the size of the absolute or relative claim it exerts upon resources is to turn our backs on the history of human progress, which has been conditioned by discovering how to do more with less and so release effort and resources from old purposes to new." The Government's intention is that, over the next four years, expenditure on this country's publicly financed health services shall rise in total by not more than about $2\frac{1}{2}\%$ per annum; but this $2\frac{1}{2}\%$ does not represent in any way the advance which these services " can, should, or will " make in those four years. The impulse and driving force that make for improvement do not arise from calculation of output or product, but from an inner compulsion. Mr. POWELL'S conclusion was that the activities

1. Memorandum of evidence to the Committee of Inquiry into the Cost of the National Health Service (the Guillebaud Committee). See *Brit. med. J.* 1954, i, Suppl. p. 69).
2. Seale, J. R. *Lancet*, Aug. 26, 1961, p. 476.

of the health service are neither justifiable by economic calculation nor assessable in comparative statistical terms; but "these are characteristics which they share with all the highest activities of man".

## Annotations

### AFTER HARVEY

FOR his Harveian oration to the Royal College of Physicians of London on Oct. 18 Sir Arthur Thomson chose a fresh theme—namely, the long delay before the significance of Harvey's work was fully revealed. Sir Charles Dodds [1] has already told us that the impact on clinical medicine was not immediate, and that, as a physician, Harvey himself went on practising traditional medicine as though he had never discovered a different kind. But Sir Arthur was concerned not so much with practice as with the consummation of a scientific idea; and he showed that we owe this consummation to a series of laboratory workers rather than to clinicians.

Whether Harvey ever wrote his intended treatise on respiration is uncertain; but it was the function of the lungs that remained so obscure. Harvey thought that their function was to get rid of heat, and he was convinced that for this purpose the blood must pass through the lungs; but he could not trace the pulmonary vessels, and their path was not demonstrated till four years after his death, by Malpighi. When Leeuwenhoek confirmed it microscopically, there could be no further doubt about the circulation of blood through the lungs. To the end of his life, however, Malpighi believed that the purpose of respiratory movements was to mix the blood, and the contrary was not proved until Hooke showed, in the dog, that muscular movement was unnecessary so long as the lungs had fresh air. Mayow went a step further by postulating a vital quality in the air—the spiritus vitalis. Further progress then depended on the chemists. Boyle, whose *Sceptical Chymist* appeared soon after Harvey's death, had done for chemistry what Harvey had done for physiology—substituting experiment for doctrine; but the phlogiston theory was still dominant and progress was slow. Cavendish isolated "inflammable air" (hydrogen); Priestley isolated oxygen from mercuric oxide; and in 1756 Black recognised a "fixed air" (carbon dioxide) produced by combustion, which he also found in air from the lung. But it remained for Lavoisier to show that lungs do not disperse heat, as Harvey thought, but create it by combustion. Not until 1862 was Pflüger in Bonn able to consummate Harvey's work by proving that oxygen was absorbed by the lungs from the air, that venous blood contained more carbon dioxide but less oxygen than arterial blood, and that the essential seat of respiration is the tissues.

The morals of this story drawn by the Harveian orator were (1) that the only sound basis for medicine is the scientific method, and (2) that it is dangerous not to question Authority. But this danger is less than formerly; for one of the disconcerting experiences of his own generation has been, he said, to find that their most authoritative utterances can be set aside by some technician in a laboratory. Disconcerting but (he felt) entirely wholesome.

1. Dodds, E. C. *Brit. med. J.* 1960, ii, 182.

### THE BOMB TESTS

ON Tuesday the Medical Research Council issued a statement on the effects of the radioactive fallout likely to be generated by recent Russian tests of nuclear weapons. The day before, a nuclear explosion detected in the area of Novaya Zemlya was reported to be of a power possibly as great as 50 megatons. And the M.R.C. statement included an assessment of the possible biological consequences of such an explosion.

The explosion of Monday's bomb seems likely to bring the total energy released from this series of tests to approximately that of all the explosions in 1957 and 1958. If the bomb was exploded in the atmosphere the resulting fallout would depend on the extent to which the energy was due to fusion rather than fission and on the altitude and site of the explosion. The explosion of such a bomb in the atmosphere in northern latitudes during the autumn could be followed by considerable fallout of shorter-lived radioisotopes. "Radioiodine deposition due to the series might then be substantially greater than that from previous tests and the contamination of milk in the subsequent weeks might cause the annual mean level to approach" 130 micromicrocuries of iodine 131 per litre. The M.R.C. have concluded that an acceptable thyroid dose would not be exceeded in any age-group of the population unless this average concentration of iodine 131 in milk was exceeded over a period of one year, or higher concentrations for correspondingly shorter times. The level has been set to provide a margin of safety for the section of the population in the group in which the dose-rate would be highest—namely, infants up to the age of 1 year. Considerably lower radiation doses would be received by older children and adults consuming the same milk. Allowance has also been made for the likely variation in the concentration of radioiodine in local milk supplies. A considerable decrease would be expected within a few weeks if tests were stopped.

When it became apparent that the new series of nuclear explosions might lead to appreciable quantities of iodine 131 in milk, the Agricultural Research Council Radiobiological Laboratory began to examine milk from 8 depots or farms in central and southern England, Wales, Scotland, and Northern Ireland. The mean results so far obtained are:

| *Week commencing* | *μμC iodine 131 per litre* |
|---|---|
| Sept. 16 | 85 |
| Sept. 24 | 109 |
| Oct. 1 | 138 |
| Oct. 8 | 150 |
| Mean for four weeks | 120 |

After the explosion of a 50-megaton bomb, radioisotopes of medium half-lives, such as zirconium 95, might be expected to raise the external radiation level in the open for some months by an amount comparable with the dose-rate received from natural sources. The statement adds that it is not yet possible to predict with any accuracy the total additional radiation dose to which the population will be committed by the current series of Russian tests, including the explosion of a 50-megaton bomb. Bone concentrations of strontium 90 in young children might rise in the course of one year to about twice the maximum level observed hitherto, but the level regarded by the Medical Research Council as the maximum permissible would not be reached. The highest fallout-rate of some of the longer-lived radioactive substances, such as strontium 90, would not be expected until the late spring of 1962.

Regular measurements of radioactivity in rain, drinking-

water, food (including milk), air, soil, vegetation, and human bone are continuing according to a country-wide programme under the supervision of the Medical Research Council and the Agricultural Research Council. The results of measurement of radioactive fallout are published at frequent intervals. "Premature attempts to interpret the significance of individual early measurements directly in terms of human hazard can be extremely misleading. Variations in the measurements are to be expected, both from day to day and as between one place and another. The significant factors are average levels over long periods of time."

## NURSING-HOMES

FEW general practitioners will be surprised to hear that all is not well in our nursing-homes. Woodroffe and Townsend [1] have described a small research project carried out at the London School of Economics between September, 1960, and May, 1961. The results, they say, "pose important general questions for the future development of social policy".

According to the Ministry of Health, in 1960 there were nearly 1200 registered nursing-homes in England and Wales with about 18,700 beds. In addition there were at least another 114 voluntary homes with some 5500 beds, which were exempt from registration. There were at least 5 nursing-home beds for every 10,000 population. The homes are concentrated mainly in the Home Counties, the dormitory areas around London, and middle-class or "retirement" areas along the coast and in the south-west of England. In many parts of the country there are few or none. The great majority of patients in nursing-homes are elderly people, and roughly three-quarters of those studied were not permanently bedridden. In their functions many nursing-homes seemed to be much the same as old people's homes. Yet there was a notable lack of sitting-rooms and dining-rooms. General practitioners who visit these homes will be familiar with the sight of relatively able-bodied old people virtually confined to bed, or at least to sitting on their beds, all day long and even for meals, because there is no room anywhere else. The report states:

"The majority of the elderly patients appeared to have few social contacts, and concern was expressed by proprietors about their social isolation. The extent to which elderly patients in Nursing Homes are isolated from the local community, or have no visiting relatives to safeguard their interests, seemed to be an important subject for enquiry."

A few of the private homes were owned by medical practitioners or limited companies, but the great majority were both owned and managed by individual women, nearly all of them qualified nurses. There were wide divergences in the attitudes of matrons to their patients. Some maintained high standards of efficiency and sympathetic nursing; others seemed to be incompetent or authoritarian and had allowed the premises to deteriorate. Local authorities varied considerably in the frequency with which they inspected the nursing-homes. A third of the homes were visited once or twice a year, but a quarter were visited four or more times.

Weekly fees in the private nursing-homes varied from £2 10s. to 27 guineas. In three-quarters of the homes the minimum fees ranged between 6 and 14 guineas, and the maximum fees between 10 and 22 guineas. Several proprietors said they were in financial difficulties, and expressed resentment at the lack of Government recognition for the service they performed in relieving the pressure on chronic sick beds of hospitals. They suggested some form of Government subsidy to enable more old people to enter or stay in nursing-homes.

The definition and classification of nursing-homes is not easy. Private convalescent homes, private old people's homes, and some guest houses and residential hotels provide similar accommodation for the same sort of people. The distinctions made by local authorities must be somewhat arbitrary and artificial. Some establishments are run as nursing-homes and yet escape registration and inspection. Voluntary homes may be exempt. There is no formal method for ensuring that the proprietor or matron is a person fit to care for the infirm and sick. Finally, the standard of amenities and staffing in a substantial proportion of nursing-homes is inadequate. Existing legislation is "extremely weak and anomalous".

There is a strong argument, supported by local authorities and the Society of Medical Officers of Health, for new legislation. The provisions in the Mental Health Act of 1959 for mental nursing-homes set an important precedent for the kind of measure that might be introduced. Such a reform, the report says, would be welcome, but would not solve certain major problems. How far, for example, could local authorities ensure that the proprietor or matron of a home was suitable for the task? To insist on a medical or nursing qualification does not appear to be enough, simply because the pecuniary rewards of running some nursing-homes may attract the wrong kind of people, and particularly those who have not been found suited to a career in the statutory health services. But the main practical objection to privately run nursing-homes is not that profits can too easily be made at the expense of the sick, but that those who manage them are free from public appointment and regular supervision.

Another problem which would not be solved by simply widening the scope of the more specific measures introduced for mental nursing-homes is that of the relation between nursing-homes and the other types of private health and welfare institutions operating outside the main health and residential services of the country. A given establishment which houses elderly people, a few of them bedfast and others in varying degrees infirm, could be a convalescent, recuperative, or rehabilitation home, a private or a voluntary nursing-home (and within either of these categories a mental nursing-home), a private old people's home, or a "Royal charter" voluntary home. According to its status it could come under any one of six separate legislative requirements, and be inspected or visited either by representatives of the regional hospital board, by the medical officer of health, by the local-authority chief welfare officer, or by none of these.

In the 19th century social work developed, and institutions were founded, on the basis of rigid classification. Nowadays human needs are recognised as much more complex than was formerly assumed, and it is increasingly difficult to place individuals in tidy categories which accord with the classification of institutions. Today people in roughly the same condition can be found in chronic sick, general, and mental hospitals, nursing-homes, old people's homes, "half-way" homes, and mental "hostels" for the aged. Many of their needs may not be met, simply because certain forms of treatment or care are not available in the particular type of institution in which they happen to live, or can be met only at the price of

1. Nursing Homes in England and Wales: a Study of Public Responsibility. By CAROLINE WOODROFFE and PETER TOWNSEND. London: National Corporation for the Care of Old People. 1961. Pp. 71. 7s. 6d.

frequent upheavals by transferring them ruthlessly from one type of institution to another as their physical and mental condition improves or deteriorates.

"The old philosophy of the institution is in the melting pot." The truth of this statement is evident from the report, which suggests that in the long run there may be advantages in setting up a regional inspectorate for all health and welfare establishments that are not owned and managed either by the regional hospital board or by the local authority.

## CONSTITUTION AND DISEASE

ONE of the occasions of London's academic autumn is the opening session of the British Postgraduate Medical Federation's annual series of lectures entitled The Scientific Basis of Medicine. Their success as spoken expositions of scientific inventiveness has been amplified by the publication of many of the past lectures in an annual volume (the latest of which is the subject of a notice on p. 965). Last week Lord Cohen of Birkenhead gave this year's first lecture, in which he examined the influence of human constitution on disease.

The historical development of ideas on this subject has been in part moulded by man's beliefs about how his body is in fact constituted. The Greeks made valid observations on the influence of physical attributes on health, and Lord Cohen quoted Hippocrates' 44th aphorism, now upheld by all life-insurance companies, to the effect that obesity shortens the expectation of life. They tried to explain the qualitative aspects of health and disease in terms of harmony or imbalance between the four humours—blood, phlegm, yellow bile, and black bile. Prominence of one of these yielded different constitutional types—the plethoric or sanguine, the phlegmatic, the bilious, the melancholic—with characteristic physical and mental features and differing susceptibility to disease. And it was a long time before this theory succumbed to mounting knowledge and the awakening of scientific method. Traces of it persist in words like melancholia (a condition attributed to excess of black bile), rheumatism (an abnormal flow of the humours), and gout (from *gutta*, a drop).

In a book [1] published in 1814 and only lately rediscovered as important work, Joseph Adams cited examples of congenital or connate diseases, and distinguished between a "disposition" to disease, when the condition inevitably appeared in later life, and a "predisposition" which required some environmental influence to make the disease manifest. Adams also recorded the evil effects of consanguinity. When Chadwick demonstrated what could be achieved by changes in environment and Pasteur set out his germ theory, interest in inheritance abated somewhat in favour of a study of external factors; but there followed Galton's fundamental work on twins and the emergence of Mendel's quantitative laws of inheritance.

Turning to the modern scene, Lord Cohen illustrated how it was becoming increasingly possible to recognise heterozygotes where the homozygotes alone show overt disease. This was especially true of inborn errors of metabolism. For example, the administration of L-phenylalanine to the parents of children with phenylketonuria produced higher serum-phenylalanine levels than normal but not so high as in frank phenylketonuria. The single-gene diseases of particulate or segregated inheritance, such as Huntington's chorea and achondroplasia, were relatively rare. The most common forms of inheritance were, both in health and disease, polygenic—i.e., a large number of genes contributed to determine a characteristic, such as height, or skin colour. The existence together in the same population of two or more variations of a physical character, or "polymorphism", was not of neutral survival value. Blood-groups or the ability to taste phenylthiocarbamide (P.T.C.) constituted a true or balanced polymorphism. Sickle-cell anæmia exemplified a "transient" polymorphism. Here a difference of a single aminoacid in the three hundred which form half a molecule of hæmoglobin produced the abnormal hæmoglobin associated with sickle-cell anæmia; the heterozygote (sickle-cell "trait") showed some protection against malaria. And Lord Cohen also referred to the interesting association between ability to taste P.T.C. and the development of multiadenomatous goitre, and between hæmolytic anæmia and deficiency of glucose-6-phosphate dehydrogenase. Study of isoniazid blood-levels in people taking this drug had shown a bimodal curve: there were apparently slow inactivators of isoniazid and rapid inactivators, and the slow inactivators were more likely to get polyneuritis as a side-effect of isoniazid treatment. Lord Cohen foresaw an exciting future for this new subject of "pharmacogenetics".

1. Adams, J. A treatise on the supposed hereditary properties of disease, containing remarks on the unfounded terrors and ill-judged cautions consequent on such erroneous opinions. London, 1814.

## COLLES' FRACTURE

WE are perhaps a shade complacent about the results of treating Colles' fractures; and, if so, this feeling is not always shared by the patient. The architecture of the wrist-joint is often restored readily enough by manipulation; but perfect reduction is seldom retained, and re-reduction is often difficult and may be followed by further displacement. It is common in these cases to ignore the radiographs and to concentrate on function, and in many patients the range of movement of the wrist-joint and the power and use of the hand return almost to normal; but, with severe and persistent displacement, movements of the wrist may be considerably impaired and the appearance of the joint be unacceptable.

An important factor governing re-dislocation of the radial fragment is comminution of the back of this bone, and the cortical defect in this region may take some time to consolidate. Charnley [1] has attempted to control this defect by packing the radius with bone chips. But such a method, even if successful, could hardly be used routinely in a fracture as common as this which is normally treated in the outpatient department.

Dowling and Sawyer [2] have described a method of pin fixation which appears to give a better chance of anatomical reduction than closed manipulation. The method consists essentially in internal fixation by a Steinmann pin, which is threaded from the distal end of the ulna obliquely, distally, and laterally to engage in the radial styloid. The arm is then immobilised in plaster for at least eight weeks. Dowling and Sawyer have compared the results of treatment in this way with those in a series of fractures previously reviewed at their hospital, and they show that there has been a considerable increase in the number of good results obtained, even though most of the patients in the recent series had severely comminuted lesions.

1. Charnley, J. The Clinical Treatment of Common Fractures. Edinburgh, 1961.
2. Dowling, J. J., Sawyer, B. *J. Bone Jt Surg.* 1961, **43A**, 657.

A better anatomical result, it was found, could usually be achieved by this method; and, although the anatomical and functional results do not correlate completely, it may be possible by this means to avert some of the gross permanent displacements which are associated with considerable deformity and disability.

## AGRICULTURAL PROBLEMS IN DEVELOPING COUNTRIES

ABOUT two-thirds of the world's population is inadequately fed. Most of these people live in developing countries in the tropics. It is probably no accident that few of these countries have reached the levels of economic development found in mid-latitudes, for undernourishment limits capacity for work and increases the incidence of disease. Great efforts have been made since the end of the war, both by national Governments and by international agencies, to improve the standard of living in these countries by raising agriculture from a subsistence economy to a commercial economy. Good progress has been made; but an enormous further increase in food production could result from a wider application of present-day knowledge, as was emphasised by Prof. R. G. Baskett in his introductory remarks as chairman of a Nutrition Society symposium on Oct. 13. Prof. L. Dudley Stamp gave an illuminating account of the climatic limitations to development in the tropics. The outstanding problem, he said, is the control of water, particularly its conservation in the arid regions. Prof. A. H. Bunting considered arable cropping, Mr. T. J. Lansbury livestock production, and Mr. R. S. Rack fishery development, each in the light of first-hand experience. Plans drawn up by F.A.O. for increasing animal production were discussed by Dr. J. C. Shaw.

The problems of arable cropping are generally more easily tackled than those of livestock production, and in the past decade the world output of arable crops has increased by more than 50%. This increase has been achieved mainly by raising the yield per acre, though the area under cultivation has been enlarged by about 10%. Not all countries have benefited equally: whereas the increases in output in China have been particularly striking, the yields in India have remained low. Professor Bunting believes that further improvements should follow the wider planting of improved crop varieties, the application of better production methods (including the use of fertilisers), and the more widespread use of agricultural chemicals to control pests both in the growing and in the harvested crop.

Livestock and fish are important as dietary sources of much-needed protein of high biological value. The predominant livestock in these regions are cattle, sheep, and goats; these ruminant animals compete less directly for human food than pigs or poultry, which, however, have their place where suitable feeds are available and where waste products can form a part of their diet. Cattle provide a means of producing human food from large areas that would be otherwise unharvested, but at present cattle production is seriously limited by wasting through shortage of food and water in the dry season. The introduction of European breeds appears to offer little advantage, for satisfactory production can be obtained with the native breeds when they are adequately fed. The real need, as both Dr. Shaw and Mr. Lansbury pointed out, is for more research on the nutritional requirements of cattle in tropical countries, on the improvement of pastures and the conservation of fodder, and on the value of non-protein nitrogen supplements to poor-quality roughages. Much progress has been made in the control of disease; and, although there is more to be done, the main factors now limiting production are nutritional.

It was made abundantly clear that the useful application of modern methods of husbandry in the developing countries must go hand-in-hand with higher educational standards and technical training, and it is here that the more highly developed countries can make their greatest contribution.

## NOBEL PRIZEWINNER

THE 1961 Nobel prize in medicine has been awarded to Dr. Georg von Békésy for his outstanding contribution to our knowledge of the transformation of mechanical energy into neural energy in the cochlea.

von Békésy has been a senior research fellow at the psycho-acoustic laboratory at Harvard since 1947. He is a physicist who was born in Hungary in 1899 and studied at the Universities of Berne and Budapest. His earlier researches from 1924 to 1946 were carried out in the Royal Hungarian Institute for Research in Telegraphy in Budapest. After this he spent a short period at the Royal Institute of Technology at Stockholm. As early as 1928 he had produced a hypothesis based on new observations which, as Wever rightly states, inaugurated the modern era of travelling-wave theories of vibration of the basilar membrane.

Largely because of the smallness of the middle ear and cochlea and the difficulties of making accurate measurements, many theories have been proposed to account for the phenomena of hearing. Békésy's contribution was to produce further facts, realising that it was useless to theorise about how the ear discriminated pitch without knowing how the vibrations produced by a sound were distributed along the length of the basilar membrane. One of his most successful methods of research has been the making of the models for which he has become famous. Sometimes these were the size of the human cochlea, but at other times large-scale models were constructed in the way that large ships are built from small models.

Békésy showed that each of the four major theoretical vibration patterns of the basilar membrane could be obtained by varying two elastic properties of the membrane and that the opposing theories shaded into one another more than had been realised. If the two variables are adjusted to their numerical values in the cochlea of a living animal or a fresh preparation of the human ear, travelling waves are observed along the membrane which have a flat maximum that shifts its location along the membrane with a change of frequency, the place of the maximum determining the pitch. Experiments using the sense of touch indicate that such flat maxima can produce quite sharp local sensations by a nervous inhibitory reaction.

Békésy's genius is shown not only in his ability to select the significant problem and his ingenuity in evolving methods to solve it, but also in a rare gift of lucid exposition, apparent in the numerous papers now fortunately gathered together in his Experiments in Hearing. This choice as Nobel prizeman will give great satisfaction to everyone concerned with the problems of hearing.

# From Words to Wards

## 1. "THE RIGHT HOSPITAL"

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A VAST programme of new hospital building in Britain is now under way. It calls for the urgent replacement of many hospitals which do not meet the requirements of modern medicine. The pressing need is for general and special hospitals with better facilities for patient care and improved arrangements for special diagnostic and therapeutic units, and for reorganised systems of supply to improve organisational efficiency. The immense investment in this programme calls for wise design to ensure efficiency, economy, and quality of building. Are we facing the challenge? Will the social historian of the future be able to look back with admiration on our planning of these new hospitals? Are our principles of planning sound? Are our horizons wide enough?

In this article we raise a number of questions on national planning policy for hospitals, outline the general aims of hospital architecture, and describe some of the difficulties in planning a new hospital. We wish to air doubts about national planning policy in the hope that subsequent discussion will result in a reassessment of national needs and the formulation of improved ways of meeting these needs. We feel that there is a great danger that our thinking may be unduly influenced by the attractions of minor improvements in hospital design, because of a failure to appreciate the extent to which our present hospitals fail to meet the demands of modern medicine. Is our thinking still too much in the 19th century? Are there adequate reasons for limiting the maximum size of a general hospital to 800 beds? Are we right to limit some of our larger hospitals to an existing site which may compel a pattern of redevelopment which will fail to meet the needs of the future?

### The Need for Understanding

Anyone who in recent years has attended meetings on future hospital design must be anxious about the answers to these questions. A visitor to such meetings cannot avoid the conclusion that the saying *quot homines, tot sententiæ* applies all too frequently to discussions on the definition of policy aims in planning our new hospitals. Yet without a clear definition of policy, the right hospital cannot be built. There are failures both in ideas and in communication, and our central theme is that a much greater effort is needed to understand the many complex problems involved in hospital design, and to break down the barriers which exist between the doctor, the administrator, and the architect.

The joint authorship of this article is significant in that it reflects the will and experience of a doctor and an architect in trying to reach a common understanding. We have had to resist the temptation each to write a separate section and pass it off as a combined article. It is a strange paradox that the medical scientist who is now familiar with cooperative inquiry and combined authorship in scientific papers should find it difficult to collaborate in the team effort required for the solution of the manifold problems in the planning of a new hospital. Likewise, the architect is too often enveloped in the stylistic problems of the building, at the expense of a close study of the needs of its users. We start, then, with the idea of close collaboration in which the vision of a service, and the vision of the building provided for it, are to some degree fused. We could not have written these words without the background of many months of inquiry, discussion, and healthy argument relating to the new teaching hospital to be built at Ninewells, Dundee.

We believe that the building of new hospitals can and should make an important contribution towards providing a much-needed sense of purpose in the bewildered society of the angry young man. More perhaps than any other type of architecture, the modern hospital should express the values of science to the physical and mental well-being of man, and the ideals of service to society. If medicine has now become a social service in Britain it is largely because it has been built on a foundation laid by enlightened individuals in this past half-century, and because it is still inspired by the great ideals of service contained in the Hippocratic Oath.

To understand the design of any building it is first necessary to recognise that architecture is a social art—an art which seeks to control technology by the application of human values to the design of buildings, their equipment, and their relation to one another and to the landscape. In the design of a hospital modern medicine places particularly heavy demands on the architect to provide a wide variety of spaces for a complex of functions, from patient care and student teaching, production processes, and supply methods to medical and scientific research. These activities have to be accommodated in an environment determined by human comfort, working efficiency, and scientific needs. Ultimate success in building the right hospital calls for cooperative endeavour by a parliament of specialists—medical, nursing, administrative, architectural, and engineering. Success entails hard work, infinite patience and great tact. Difficulties and misunderstandings can be reduced by an appreciation of the functional, organisational, and architectural aspects of the design problem. Increasing specialisation with its accompaniment—technical jargon—inevitably leads to difficulties of communication at committees. The differences of opinion which all too often engender heat at committees can be overcome only by small group discussions between a small planning team and interested specialists. It is helpful to bear in mind during discussions that primarily the doctor is concerned with the operational efficiency of units of accommodation in the interests of the wellbeing of his patients; the administrator with the efficient organisation of limited resources and with their distribution to achieve the maximum result with the minimum of effort; and the architect with the design of an interior and exterior environment which will meet the physical and emotional needs of the users. All should strive to attain to what Sir Patrick Geddes, professional botanist turned pioneer town-planner, called the "synoptic view". The final design of a hospital is the fusion into a composite whole of the exacting requirements of many specialists.

It is helpful if those responsible for the planning of a new hospital understand not only the necessity to define the problem but also the ways in which the architect approaches the creative process of design.

### Three Phases

At the beginning of the process is the period of investigation, when doctor, administrator, and architect are studying the functional requirements. This is very much a phase of inquiry and analysis into reasons and attitudes and behaviour leading to measurable factors in relation to a given function. It involves the assessment of numbers and categories of staff, their activities and movements from place to place, the equipment they use, and the nature and degree of control of the environment which they require. From a clear and precise statement of people, processes, and organisation emerges the brief; it should be noted that this is much more than a schedule of accommodation.

The next phase is that of architectural design when functional requirements are interpreted in terms of space and environment. This phase represents the synthesis of ideas when the environment needed is given shape and form, and a sense of purpose.

The third phase is the production of the building, its mechanical services, equipment, furniture, and landscape. This phase requires a clear and undivided organisation in which the designer and constructor are allowed to complete the building speedily, economically, and without interruption. That this is rarely achieved is usually explained by a failure in the two preceding phases.

In these three phases the communication of ideas and the giving of explanations and instructions play a vital role. If the language used is not understood, then delays and ultimate failure may well ensue. Words often present difficulties with terminology, and in some ways they are of limited use. Drawings and diagrams can give a clear visual impression of certain problems apart from illustrating in two dimensions the disposition and arrangement of units of space and the movement of people or things in space. The essential architectural solution, however, of how space is enclosed, and how it relates to structure, equipment, and sources of light, &c, can only be demonstrated by models. These techniques, therefore, form the language in all phases of the creative process.

### Adaptability

Good planning demands an analysis of changing needs in the future. Lack of imagination now could mean leaving a poor legacy to our successors. Rapid progress in medical science and in the application of industrial methods to hospitals, and the rising standard of living, are the three major aspects of the potential for change. The oft-quoted phrase that a hospital is out of date on the day it opens would only imply failure if there was inadequate capacity to meet changing needs.

Louis Sullivan, the great American architect of the 19th century, said: "Form follows function." The processes of change, technical, economic, and social, are now so greatly accelerated that most buildings must be given some "built-in" capacity to accommodate the changes without undue strain. They should not be tailor-made to fit one set of functions at the outset. The building should fit rather loosely the type of work, organisation, and environment for which it is designed. The form should not be restricting to future change.

The searching question here is how to predict just where all new requirements may arise. The much-used word "flexibility" is often employed to cover lack of precision in thinking. Strictly speaking "flexibility" in relation to building design means an extensive capacity to alter and extend a building to suit changing needs. It, therefore, involves not only demountable construction but the facility to make extensive alterations to the mechanical services. Such "flexible" structures have been designed for industrial and military projects, but usually for the simplest of functions with relatively simple mechanical services. To apply this approach to such a complex building as a hospital, even if the many technical problems of construction and services could be solved, would be very expensive.

What is needed is better described by the word "adaptability". An adaptable building is one to which internal adjustments can be made in response to changing needs and which can be extended externally. Adaptability may not be as difficult to achieve as it seems, for it depends largely on planning techniques relative to four aspects of change:

(*a*) Redistribution of people within the existing unit of accommodation. This can mean the movement of some equipment and some change in the function of rooms within the broad category of work for which they are designed.

(*b*) Overflowing of an expanding unit of accommodation into an adjoining one—i.e., decanting. This requires a basic similarity in design, layout, and services in the units of accommodation concerned.

(*c*) Extension of a particular unit of accommodation by additional building. This requires well-organised lines of communication and piped services along which the building can grow.

(*d*) Alterations in the design and use of equipment which, within reasonable limits, can be met by a simple repetitive arrangement of services.

To achieve this quality of adaptability in the building requires especial care in compiling the brief, and a clear decision on policy, with much thought given to the possibilities of standardisation and future growth. It requires strong architectural control with cohesion and firmness in the design. Often lack of such control results in a poor meaningless building. In recognising this problem of change and development one must also attempt to reveal the ways in which the hospital service is likely to develop—to identify, in other words, the points of growth. The great danger is to underestimate the speed of development of modern technology. This poses many questions and demands a certain amount of gazing at the horizon. To use this metaphor is not to suggest that it is all a matter of guesswork. Very little of it need in fact be guesswork. Certainly we need perception to see things as they are, and imagination to see them as they might be, but the use of these qualities must be wedded to systematic study of problems and needs, of theory and the application of ideas. There are many questions now being asked to which there are as yet no apparently satisfactory answers. Should the major hospitals represent all specialties on one site? What hospital services should remain at the local level? What should be centralised in the larger cities? Are we providing enough laboratory facilities for clinical research in every hospital? How much can the out-

patient services expand, and the inpatient beds contract? Will the production and supply departments be organised more on a regional basis? Will they necessarily be attached to any one hospital or group of hospitals? How is the student to be presented with the whole medical problem, not just fragments of it? Will the traditional pattern of clinical charges be replaced gradually by a more collaborative pattern of medico-surgical teams?

### Unanswered Questions

These and many other questions require extensive study before a consistent policy on hospital planning emerges. With such a policy we should have more confidence in what we provide. But we still need to know much more about how to provide it, about the wide range of design problems for which performance standards are imperfect or vaguely understood. To take one example: how much misunderstanding is created in the discussion of the controlled internal climate? The very words " mechanical ventilation " seem to raise unnecessary prejudice and speculation, and yet without such ventilation control of the internal climate of a hospital is impossible.

The uncertainties in planning policy and in the architectural design of a hospital are the main factors contributing to the long time it takes to build a hospital. They are often revealed in the finished product, in its lack of " commodity, firmness and delight ".

As is apparent, we have asked more questions than we have attempted to answer. The fact that readily accepted answers are not available indicates the amount of fundamental thinking yet to be done. We would, therefore, like to make a plea for the early establishment of a research organisation with adequate resources to initiate experimental inquiry and field studies, and with the freedom of action customarily permitted to research councils.

## Special Articles

## GENERAL-PRACTITIONER-OBSTETRICIAN UNITS

FROM A CORRESPONDENT

A meeting held by the Royal College of Obstetricians and Gynæcologists on Oct. 18, under the chairmanship of Sir ANDREW CLAYE, included a discussion of the staffing and management of general-practitioner-obstetrician units and the part these should play in the obstetric services.

General-practitioner beds have come to stay, said Mr. JOHN STALLWORTHY (Oxford). There was no disagreement with this, either as a statement of fact or as a statement of future policy. There was, however, much less agreement about how these beds should be staffed and managed.

Any hint of complacency was skilfully shattered by Dr. NEVILLE BUTLER, director of the National Birthday Trust Fund survey of perinatal mortality. Simply and convincingly he presented figures to show that there is room for a very great deal of improvement. Dr. Butler's figures were based on a sample of all deliveries which took place in one week in 1958. 1 in 8 of them took place in a G.P. unit without a resident medical officer. He pointed out that these units usually also lack amenities for blood-transfusion in an emergency or for rapid cæsarean section. But what is serious is not so much the lack of facilities for dealing with emergencies as the fact that G.P. units appear to be booking the same sort of cases as consultant units. In 1958 women with known high risk of perinatal loss were commonly booked in G.P. units. High-risk mothers, such as primiparæ over the age of 30, women over the age of 35, and grand multiparæ, formed 15% of all cases confined in G.P. units. If all other primiparæ, being also a known high-risk group, were considered as candidates for delivery in units with resident medical officers, then the proportion of high-risk bookings in G.P. units on grounds of age and parity alone exceeded 60%.

Does this really matter? asked Dr. Butler, and proceeded to give an incontrovertible answer. These 15% made up nearly a quarter of 480 perinatal deaths in G.P. cases booked and delivered in such units.

The survey also showed that in many G.P. units antenatal care was of poor quality. The hæmoglobin was not estimated in 46% of cases and the rhesus group in 5%. In 16% the blood-pressure was not taken on every visit in pregnancy. All this approximated more to the antenatal care received by domiciliary booked cases than to those booked for consultant units, in spite of the proportion of high-risk patients already shown to be booked at G.P. units. A scrutiny of the deaths showed also that in many cases toxæmia was not diagnosed, nor treatment started, early enough, and that many such cases were not transferred to consultant units for treatment and delivery.

The way in which G.P. units can and have been organised satisfactorily was shown by Mr. STALLWORTHY. An important factor, he said, is the spread of a consultant's influence (rather than his actual powers) outside his immediate sphere. In the Oxford region G.P. units are widely used and highly organised, with close liaison with the parent hospitals. It has been found to be of the utmost importance to have consultant visits and flying-squads organised by the hospitals. It is extremely important, too, that the G.P. unit should produce annual reports so that those working there can know not only what they think they have done but also what they have in fact done. Liaison is also improved by regular regional clinical meetings. Organised in this way, the G.P. units in the Oxford region halved their total fœtal mortality between 1955 and 1960. The latest figures show that 5000 mothers have been delivered with only 1 maternal death and a perinatal mortality rate of 13 per 1000 live and still births, compared with the national figure of 35. One of these G.P. units, at Savernake Hospital, was described by Dr. T. A. MAURICE, a general practitioner who works there. This was followed up by accounts from Mr R. A. TENNENT, Dr. P. B. BAILEY, and Mr. NEVILLE HART, who described what is being done in the G.P. units in Lanark, Bristol and Bolton.

General practitioners who took part in the discussion expressed doubt and concern on a number of points. One of these was whether G.P. units should be " open " to all general practitioners who wish to deliver their cases there, or whether they should be " closed " and used only by general practitioners who have been elected to the staff and who take their turn in a rota of duties. In practice, " open " units are usually for general practitioners delivering their own patients, for which they are paid by the executive council. " Closed " units are more closely connected with hospitals, and the G.P.s who work there are paid on a sessional basis. One questioner expressed the view that a " closed " unit such as that at Savernake described by Dr. Maurice, might easily come to mean " closed shop ". Dr. MAURICE denied this, and Mr. STALLWORTHY emphasised that consultants are visitors and not directors in these units.

Closely allied with this problem was the question of how much a general practitioner should specialise in obstetrics, how much discipline he should be prepared to accept, and how much is needed.

Dr. Butler's figures showed that in many places a change of practice is needed, and the experience of the Oxford region and elsewhere shows how improvements can be made. Unfortunately there was no discussion of the very different problems involved in densely populated areas such as London which at present have a negligible number of G.P. beds, and where the maternity services are severely strained by the rising birth-rate, the increase of population (particularly through immigration), and the enormous number of late bookings and emergencies. It would seem that these areas are most in need of G.P. units but are worst served, and this may be an important reason why the maternity services in these areas are in such an unfortunate and even dangerous condition.

## THE CHEMISTS AND THE N.H.S.

Last week the Minister of Health told the Central N.H.S. (Chemist Contractors) Committee that he could no longer delay introducing revised rates of payment to chemist contractors in England and Wales. The following new rates will come into effect for prescriptions dispensed on and after Nov. 1:

| | *Present rates* | *New rates* |
|---|---|---|
| Average dispensing fee per prescription | 14·7*d.* | 17·1*d.* |
| "On-cost" allowance (i.e., percentage on ingredient cost of prescriptions) | 25% | A sliding scale, designed to produce an average of 18% overall, based on 25% on first 500 prescriptions per month; 20% on next 250; 12½% on the rest. |
| "Urgent" prescriptions .. .. | 1*s.* | 1*s.* 6*d.* |
| Rota service outside normal hours of business: | | |
| (*a*) early closing day .. .. | 7*s.* an hour | 20*s.* an hour |
| (*b*) other weekdays .. .. .. | 7*s.* an hour | 10*s.* an hour |
| (*c*) Sundays and public holidays .. | 12*s.* 6*d.* an hour | 20*s.* an hour |

The effect of the new rates will be to reduce the estimated total net profit of chemists from National Health Service business by rather over £1½ million a year. It will leave total net profits on National Health Service business about 14% above what they were in 1957. A Ministry statement says that the new sliding scale, coupled with the increased average dispensing fee, will work to the advantage of the small pharmacies: it is estimated that some 4000 will be unaffected or will benefit from the new rates.

In an annotation last week we referred to some of the events that led to the committee's decision not to enter into any further discussion unless the principle of a professional fee was first conceded. The Minister then decided that he had no alternative but to introduce the new rates of remuneration as soon as possible. But the Ministry statement added that he appreciated "the importance attached by the chemists to the recognition of the professional character of their service in the National Health Service, and he has therefore offered to explore with them the possibility of redistributing the different elements in their remuneration in such a way as to give this recognition." The Central Committee will probably now call a conference to discuss a proposed withdrawal of chemists from the N.H.S.

# Occasional Book

## RECONSTRUCTING THE N.H.S.?

CONTROVERSIAL opinions on the health services were expressed by Dr. D. S. Lees (senior lecturer in economics at the University College of North Staffordshire) in his articles in *Lloyds Bank Review* (April, 1960) and *The Times* (March 22, 1961). This week the Institute of Economic Affairs publishes a much fuller analysis by Lees [1] which will cause comment because his criticisms are so severe and his recommendations so far-reaching.

As one who has taken a particular interest in the economics and operation of the National Health Service, I welcome the opportunity to discuss his analysis and recommendations in relation to my own.

Both Lees and I disagree with the verdict of the Guillebaud Committee that "the structure of the National Health Service laid down in the Acts of 1946 and 1947 was framed broadly on sound lines" and that "it would be altogether premature at the present time to propose any fundamental change". Furthermore, our analyses of the defects of the structure and operation of the N.H.S. are similar. To remedy them Lees would like to see medical care financed primarily by private insurance and direct payments by patients, supplemented by cash benefits from the State to those who cannot provide for themselves. My view,[2] however, is that the N.H.S. can be greatly improved even though it is still financed primarily by taxes and most medical care is obtainable by patients without direct charge.

Once it is agreed that the present structure of the service is unsound, there may well be several different ways of improving it which could be equally effective.

### INADEQUATE ANALYSES

The N.H.S. has suffered from the idea that better medical care reduces the need for further medical care. As Lees says:

"... there was a widespread belief when N.H.S. was founded that the amount of sickness in society could be reduced simply by ensuring an appropriate amount and organisation of medical services. In the Beveridge Report of 1942, for example, it was assumed that the cost would not rise, the prevailing opinion being that, in the long run, the cost would fall as sickness was cleared away. N.H.S. was seen as a self-liquidating institution. ... It is widely agreed that this original assumption of N.H.S. was a major error." (p. 28.)

The failure of the cost to comply with the predictions of the Beveridge report led to the myth prevalent in the 1950s that expenditure was excessive:

"Owing to gross under-estimating and subsequent inflation, N.H.S. in its early years operated in an atmosphere of financial crisis that is even now not completely dispelled. Yet when account is taken of rising prices and comparisons made with other social services and with the gross national product (G.N.P.) the increase in health expenditure is far from frightening. Between 1949–50 and 1959–60 ... health expenditure fell as a proportion of social service expenditure from 28 to 23 per cent, and as a proportion of gross national product from 4·0 to 3·9 per cent." (p. 8.)

Nor is expenditure on medical care in Britain excessive by comparison with other nations:

"... health services take a larger share of G.N.P. in the

1. Lees, D. S. Health Through Choice: an economic study of the British National Health Service. Hobart paper 14. London: Institute of Economic Affairs, 66A, Eaton Square, S.W.1. 1961. Pp. 63. 7*s.* 6*d.*
2. Seale, J. R. *Lancet*, August 26, 1961, p. 476.

United States than in Britain and, further, that share has increased sharply whereas in Britain it has at best remained constant. . . . International comparisons are fraught with difficulties in health as in other matters, so American experience cannot be taken as conclusive. But there are good reasons for supposing that it sets a natural pattern for countries with high and growing levels of wealth. In technical terms, medical care is a commodity with a high income-elasticity of demand: as incomes rise, demand will rise more than in proportion." (p. 37.)

This conclusion is consistent with my theory of national expenditure on medical care in which I stated that a persistent rise in real per-capita gross national product will tend to result in an increase in the proportion of the gross national product spent on medical care.[3] Lees may well be correct when he says: " Far from being extravagant, expenditure on N.H.S. has been less than consumers would probably have chosen to spend in a free market." (p. 58.)

The rise in the cost of drugs has not been so striking as is sometimes supposed:

" As a proportion of total expenditure, [on the N.H.S.] prescription costs as a whole have been constant since 1951–52 at between 10 and 11 per cent. . . . Furthermore, expenditure on drugs as a proportion of income is lower in Britain than in most other comparable countries and drugs prices are well below those in Switzerland, Belgium and West Germany. It would seem that much of the furore over drug costs has been misplaced." (p. 9.)

### SUPPLY OF DOCTORS

Analyses of the future supply of doctors have also been inadequate. The failure in the supply of young British doctors in almost all branches of medicine is becoming so obvious that one is surprised to remember that only 18 months ago the Royal Commission on doctors' pay said that " the supply of candidates for training as doctors is reasonably close to requirements and the question of using remuneration as an instrument either for encouraging a greater flow of potential doctors or reducing the present flow, does not arise ".

It has become customary to attribute this emerging shortage to the Willink Committee's recommendation that the intake of medical students should be cut by 10% from 1957. But the shortage has appeared before this recommendation could have had any effect on the output of doctors. The Committee did not cause the shortage, though their report will aggravate it in the future.

As in the case of costs there has been failure to understand the factors determining the supply of doctors.

" N.H.S. was fortunate in its early years in working with an increasing number of doctors. Intake into the medical schools was maintained during the war and rose sharply in the post-war years. By 1950 the number of full-time medical students was 20 per cent larger than in 1938. This was interpreted . . . as an index of the popularity of N.H.S. among doctors." (p. 40.)

In fact this plentiful supply was unrelated to the existence of the service, which merely inherited the effects of two world wars on medical manpower—namely, a large number of young doctors produced in response to World War II, seeking employment before the retirement of the many doctors produced in the years following World War I.[4] Nevertheless, there is no doubt that the severity of the shortage of British doctors which is now emerging is partly due to the existence of, and policies in the N.H.S.

3. Seale, J. R. *ibid.* 1959, ii, 555.
4. Seale, J. R. *Brit. med. J.* 1961, i, 203.

### DEFECTS OF STRUCTURE

The disadvantages of centralisation of power in the service is a recurrent theme:

" Medical care was brought under public control ' at a time when various industries were nationalised as a practical expression of the belief current between the 1930's and the early 1950's that administration is everything and large-scale organisations are more efficient than small '." (p. 21.) In the N.H.S. there is " extreme concentration of power in the hands of the Minister. . . . For all practical purposes, N.H.S. is a complete monopoly. . . . Other nationalised industries monopolise the supply of their respective products but all of them compete with reasonably close substitutes and for some of them international trade provides . . . a further source of competition. Competitive forces thus exert a constant pressure on these industries to improve quality and keep down costs or to expose poor performance. In N.H.S. the absence of built-in forces making for improvements in quality and efficiency is one of its most serious weaknesses. From this point of view, medical care is one of the last commodities that should be monopolised by the State. Power is being disciplined by decentralisation in other nationalised industries; the need for this discipline is paramount in medical care " (p. 29).

Lees is aware how intimately the method of administration is linked with the method of finance.

" It is at least doubtful if any change of substance can be made as long as medical costs are met predominately by central taxation. Little freedom from central control can be expected while the ' 100 per cent subsidy ' system continues. Tight political control follows as a matter of course from the need to ensure proper use of not unlimited public funds. Without independent sources of finance, centralised decisions must dominate the field." (p. 30.)

The heavy centralisation of power in the health service affects the quality of the medical care which it can provide.

" It is too often assumed that the capacity for good government is unlimited, that the decisions required of politicians and their advisors can be increased indefinitely in number without effecting their quality. But if Ministerial control and responsibility are to remain, the process soon runs into diminishing returns. More and more decisions have to be made in less and less time. It is a commonplace in business that when a firm is constantly working to the limits of capacity the quality of output tends to fall. The same happens in government." (p. 17.)

### MEDICAL PROFESSION

Doctors will be interested to hear what an outsider has to say about the effect the N.H.S. has had on their profession:

" The N.H.S. has created discontented professions, particularly in matters of remuneration. Successive Ministers of Health have used their extraordinary power to exploit doctors and dentists in the interests of general financial stability. That power would be better abolished." (p. 59.)

As taxpayers, we are often inclined to think that the Government is very liberal with our money. It is therefore salutary to be reminded that " twenty years of sharply rising public expenditure have tended to obscure the fact that governments can be mean as well as generous ". This is illustrated by the history of doctors' incomes since 1948:

" The Danckwerts Award restored the average real incomes of G.P.'s in 1950–51 to their pre-war level. From then on these incomes were eroded by inflation. By 1959 their average earnings had increased by 9 per cent but prices went up by one-third, reducing the real value of incomes by some 20 per cent. During the same period, the general standard of living of the community, measured by G.N.P. per head at constant factor cost, rose by 22 per cent. In short, the standard of

living of G.P.'s went down by a fifth while that of the community in general went up by about as much. Even though the Royal Commission's recommendations for increased remuneration have now been implemented, doctors are still no better off than they were ten years ago. It is doubtful if this can be said of any other section of the working community and contrasts strongly with the trend of medical incomes in most other countries. Doctors may well look askance at the assurance of Professor Titmuss in 1957 that 'whatever else may be said about the National Health Service, it can at least be concluded that, under the new regime, doctors have prospered'." (p. 44.)

Although Lees does not give examples, several grades of doctors in the hospital service are still considerably worse off than they were thirteen years ago. In 1948 a fourth-year senior registrar received £1300 per annum and today he receives £1800. At constant 1948 prices his present-day salary is only worth £1120. This means that, even after the Royal Commission, the income of a fourth-year senior registrar is still 14% below what it was just after the N.H.S. came into existence.

A fall in real earnings has been characteristic of most professions in the N.H.S.—not only of doctors. The real earnings obtainable in all posts open to State-registered nurses in the hospitals fell sharply after 1949, and none rose again to the 1949 level for ten years.

### RECOMMENDATIONS AND ASSUMPTIONS

"The fundamental weaknesses of N.H.S. are the dominance of political decisions, the absence of built-in forces making for improvement and the removal of the test of the market. These defects bring dangers for the quality of medical care that cannot be removed without far reaching reform. . . . My verdict would be that a monolithic structure financed by taxation is ill-suited to a service in which the personal element is so strong, in which rapid advances in knowledge require flexibility and freedom to experiment, and for which consumer demand can be expected to increase with growing prosperity." (p. 60.) The service has given rise to problems which "are increasing in number and complexity. On the longer view, the most acute danger of N.H.S. is that it will prevent the emergence of more effective methods of medical care" (p. 61).

It is too often forgotten by those who favour the N.H.S. in its present form that it is quite simple to produce a health service which is "free" in that the patient does not pay for his illness. The real problem is how to produce one which provides medical care of high quality, both now and in the future. Much medical care of very high quality is available in the N.H.S., but as Lees says we do not know to what extent it is living on "the skills, attitudes and loyalties inherited from the past".

To remedy the defects, Lees would diminish the role of political decisions, would remove general taxation as the major source of N.H.S. funds, and would disperse the control of hospital services away from the central Government. With these aims I am in agreement. To achieve them he would finance medical care primarily by private insurance and by direct payment by patients, supplemented by cash benefits to those who cannot afford them.

Though I believe that private health insurance will and should expand, and that private practice provides a valuable balance to a public service, I also believe that most medical services should be available free of direct charge to patients. Disputes over these matters are often disputes over value judgments, and discussion tends to be sterile. I shall therefore confine myself to questioning the validity of some assumptions on which Lees bases his proposals to increase direct payments by patients.

"Medical care", he says, "is a personal consumption good, not markedly different from the generality of goods bought by consumers." He therefore thinks it reasonable that "institutions providing medical care should charge for their services and vary supply in accordance with consumer's choice". Finally, he assures us that medical care is "something highly to be desired".

From my experience as a doctor, the statements that medical care does not differ from other consumption goods, that people choose to consume it, and that it is highly to be desired, seem major over-simplifications. The difference between medical-care goods and services from most goods and services is that usually *people do not want to consume them at all.* Most people would rather not use medical-care services; they would happily do without them even though they do not have to pay.

"Shall I go for a holiday in the South of France; or shall I buy a suit; or shall I buy a washing machine?" Here are three consumption goods all of which are desirable, about which one can come to a decision after balancing price against personal preferences, and then choose which to purchase. Similarly, consumer choice can be said to operate in minor maladies like treatment for varicose veins, or the use of luxury services such as taking an ambulance when one could well take a bus. But if one throws in another possibility, "Or shall I have the carcinoma removed from my stomach?" a choice of a different nature arises—because of the violent emotions involved and because most of all one would rather not have the carcinoma. The consumer's attitude to many medical-care "goods" is quite different to his attitude towards other goods.

It would be reasonable to say that fire-insurance is a consumer service which one chooses to purchase. Nevertheless, most purchasers hope that the house will not burn down. If it does, it would be unreasonable to suggest that the householder (or consumer) chose to have the fire; for arson, like malingering, is relatively uncommon. He chose the insurance policy—not the fire. Similarly, people choose to insure, or to be taxed against medical-care expenses; they do not choose to have chronic bronchitis, or infantile eczema, or a coronary thrombosis, or some other disorder which a person usually requires before becoming a consumer of medical care.

In buying most goods, one knows what one is buying and what one is going to pay. But patients are often swept into consumption of medical care by forces largely beyond their control, with no way of knowing how great the cost will be. Hence they wish to prepay for their medical care (whether by insurance or by taxation), and this wish is reinforced by the fact that the distribution of ill-health throughout the population is grossly inequitable. If payment is by insurance, patients do not want to be ruined financially merely because they have a chronic illness or a severe one and the insurance cover runs out, as often happens today in the United States. Indeed, they wish out-of-pocket expenses when ill to be reduced to a minimum. Therefore they want their insurance to be "comprehensive". But the more comprehensive the insurance becomes, the less does the price system of the market operate, because the consumer of medical care does not pay for it—the insurance organisation does. Yet it is the price system of the market which Lees wants restored.

Many people will have serious doubts about the desirability of some of his proposals, but none will doubt the importance of the issues the book raises.

J. R. SEALE
M.D. Cantab., M.R.C.P.

# In England Now

*A Running Commentary by Peripatetic Correspondents*

"Full pronation of the radius and ulna of the dispensing forearm, please!" said Ananias to Macabre the pathologist. "Unless these joints are put through their full range of movement troublesome adhesions form between the guest's tongue and hard palate. This beer isn't all it might be, either. I mean it might be a whole pint instead of a half, but it's vastly preferable, quite apart from the fact it's free, to the suds sold down the road at the Three Jolly Embalmers. There, the S.G. is so low that the froth sinks to the bottom, and if you're unprepared and sucking it down hard to avoid tasting it, you feel like a ship when the screws start to race clear of the water. Severe rigors and rivets starting all over the place . . . "

"If I wasn't your unfortunate host," said Macabre crossly, "you could collect your rivets and navigate your ill-found hulk out of here. As it is, do you know anything about a full bottle of gin disappearing from my room yesterday? I saw one just now on your mantelpiece."

"As that one is nearly empty and you describe yours as full," replied Ananias, "they are obviously different bottles. Really Mac., for a gaffe like that a C.I.D. man would be back on the beat tomorrow, slipping his discs heaving Lord Russell about. Put these unworthy suspicions behind you and strive to emulate your predecessor here who gladdened our hearts with his Heavy Gin, manufactured by spinning it down in the centrifuge. We ate it with a knife and fork and a dash of mescaline and after three mouthfuls the mass went critical and you felt as if you'd been exploded in Novaya Zemlya. Try it sometime, and escape from the accidie caused by overmuch necrophilic legerdemainary in a haze of Charnel No. 5. It gets all you pathologists eventually, like your forensic colleague up in Caledonia stern and wild, and justifiably so since he invented a breathalyser disguised as a set of bagpipes. It measured the amount of breath in your alcohol and was intended to trap participants in such tribal rites as Hogmanay and Burns Night. The inventor disappeared completely and the next stock-take at the pathological museum showed 17 extra pots nobody could account for . . . "

* * *

The lane up to the bungalow has great pot-holes, worn by Ralph's all-purpose lorry, and these holes have been unevenly filled with broken bricks. Darkness lent no softness to the jolts. I pulled into the yard between the lorry and a pile of scrap. I stepped out on to an oven shelf and stumbled through other assorted junk to the back door of the house. A frenzied welcome from a dog of sorts in the dark of the kitchen held up my progress, but I fought through to the hall and followed a shaft of light to the bedroom. Ralph stood by the bed, his shadow huge against the wall. His wife Clara lay all curlers and misery amongst the blankets. She was too ill to do the honours. Any suspicion of a glad eye is weighty evidence against an acute condition. (Women doctors will find this to apply the other way round.) Anyway, this was a clear-cut appendix and presented no problem for the sluggish thought processes of the small hours; but like measles, it's such a regular that one longs for some entirely new common illnesses. I followed Ralph out into the kitchen; he flung the dog out of the back door and lit a candle over the sink. Suddenly Clara was with us, stood for a frantic second grasping the front of her nightdress, and as suddenly disappeared out into the yard. The dog took the opportunity to come in again. "Hey, Doc," said Ralph, "should she be going out there?" It transpired that she had been on her way to the lavatory to be sick. Few houses have chambers, these days; this one had not even a bucket. We found a smallish pudding-basin and a plastic wastepaper basket and settled for the latter. On the way home, I wondered how the ambulance men would get on.

* * *

They were a pair of delightful little twin sisters. Both looked like tiny angels with golden hair and innocent faces. But one had acquired (with masterly skill) a very large dose of "oblivon-sweeties" and sampled them. They were both too young and frightened to say who was guilty. But the one I examined first was far from being composed, while her sister looked on from her mother's lap as happy and carefree as could be. She was obviously, I thought, tranquillised. But when it came to her turn she was worse than the first, and her sister soon snuggled down peacefully with a kiss and a cuddle from Mum.

Well, they looked alike, smiled alike, cried alike, walked alike, talked alike—and bless their little hearts—they both had a nasty gastric washout alike. It's a hard life being a twin.

* * *

Being a grass-widower, because my wife has gone to visit friends in Germany, has its complications. The domestic ones are not so bad. I can cook and do the more essential chores, though our spasmodic "daily" has, of course, chosen this month for one of her absentee spells. The worst domestic, or para-domestic, sequel has been the clouding of the previously sunny relations between myself and the manageress of the local laundry. Hitherto I would just deliver the soiled and collect the clean parcels of the household linen and my shirts and collars. All was, if not nods and becks and wreathed smiles, cheery mutual felicitations on the weather. Now, alas, I have become involved on my wife's behalf in the prolonged tussle over a teacloth missing since April. Last time, I even had to remind the manageress of our laundry-mark number.

The social effects of my wife's absence, apart from the blessed liberation of the telephone from her girl-friends' endless conversations, are a number of invitations to dinner: some of these carefully planted before her departure by my wife remarking ruefully to her friends how much she hated leaving me to cope unaided, "but, mercifully, the poor man can cook himself an egg"; some the result of friends who rang up hoping to invite both of us and got stuck with only me. Among the latter group my light-hearted account of my wife's reasons for taking a holiday without me seem not quite to carry conviction. They smile politely, but "never thought it would last" is what their eyes convey.

* * *

*News from school.*—"There's a new ten shilling note coming out on Thursday. I wonder what it looks like?"

* * *

The surgery performed each week upon my shirt by the local laundry is gaining in scope and imagination. There's a chap on the unit there who clearly believes some form of treatment to be necessary in all cases of midline excrescence (buttons to you). At first he practised simple crushing, with or without removal of fragments. Later, with improved technique, he achieved a nice little operation which reduced the diameter of the button by half, while preserving its essentially circular outline. Absence of residual function was total. In long-standing cases, where these conservative measures had failed—and they were usually sufficient in themselves to achieve spontaneous resolution of the button in time—he liked to employ straightforward (classical) amputation at the pedicle. His ultimate refinement (case discharged to home care yesterday) turns out to be removal of button with wide local excision of surrounding shirt. No attempt, I need add, had been made to bring the edges together, or at grafting. I complained about this one. But it is apparently the treatment of choice once senile changes have set in. At any rate, according to Fred Press, Director of Studies at the Laundry.

My new shirt is provocatively, nay, offensively immaculate. The buttons on it should present a multitude of problems to gladden the hearts and stimulate the minds of these anonymous *chirurgiens manqués* who lurk in the steaming subtropical vapour of laundries, quietly sublimating their urges in this annoying way.

* * *

When your tremor's approaching paresis,
A trump card if you meet the police is:
You surely don't think
That I'd sink
To the drink?
It's my dysdiadochokinesis"!

# Letters to the Editor

## DELIBERATE EMERGENCIES

SIR,—It is about time we faced up to the problem of the "E.B.S. obstetric case" and you do well to ventilate this subject in your columns (Oct. 14). Those involved in the care of expectant mothers living in the more densely populated parts of London know the difficulties only too well. All of us—the hospital obstetrician, the G.P., the public-health doctor, and the midwife—are to blame for accepting what can only be described as a travesty of modern medicine. The Ministry of Health seem remarkably silent about this major blot on the N.H.S. Perhaps the only innocent party to all this is the Emergency Bed Service itself. A voluntary body, it undertook some five years ago to help as best it could with the difficulties of the unbooked woman in labour. Having no power to insist that a hospital accept a patient, it is remarkable that it has coped so well without any authority to back it up.

Before seeking a solution we should first analyse just what the problem is, for those not directly involved may not realise what all the fuss is about. In most areas of the country those women who have some obstetric complication—e.g., hypertension or a small pelvis—or who have a previous history of obstetric difficulties are booked for delivery at a hospital. In addition those mothers whose homes are inadequate are also booked at hospital. The rest of the hospital beds are offered to those mothers who prefer hospital to home confinement, on the basis, presumably, of first come first served. In London the demand for beds by those who need them is so great that there are not enough beds to go round. In some hospitals all the beds are booked before the 13th week. Those who come to book later, however great their need, have to be rejected. It is only fair to add that those with really severe complications usually manage to find room somewhere; but for those with inadequate housing the solution is not so easy, and the degree of inadequacy has to be seen to be realised. These mothers are given what has come to be colloquially called "a booking on the E.B.S.". In fact, the E.B.S. having no beds at its disposal, what happens is that when she goes into labour the patient calls in her G.P. (or a G.P.-obstetrician) who confirms the onset of labour. He contacts the E.B.S. who *then* start to find a bed in hospital. Many mothers in these circumstances being multiparæ, the baby is often born before the arrival of the ambulance, which does not set out until a bed has been found. This means that the delivery is conducted without a midwife or equipment; and usually without a doctor. Ambulance men in London have to deliver so many babies by themselves that they carry (unofficially, I am told) the necessary instruments! Those mothers with obstetric complications—even though they had been recognised before and might have been preventable—form a large proportion of the emergencies seen in London obstetric wards today. The mother arrives *in labour* at a hospital which has never seen her before (unless the same thing happened in a previous pregnancy). If the mother has had antenatal attention from the local clinic or a G.P. she may have a special card giving details of her blood-group and the findings at clinical examinations, &c., but in the rush it is often left behind; all too frequently it is non-existent.

By normal standards there are enough obstetric beds in the London area to meet the theoretical requirements, assuming that the criteria laid down by the Cranbrook Committee are adopted. But the overcrowding in Central London has led to a higher proportion than average of mothers needing a bed in hospital. To this increased demand must be added the unmarried mothers who flock to London from all parts of the country, and the already pregnant immigrant mothers who invariably find themselves homes totally unsuitable for delivering a baby. If we then deduct from the number of available beds those occupied by mothers sent from the provinces to the teaching hospitals for the special treatment that can only be found there, it is not surprising that last year about 4000 women went into labour without any adequate arrangements being made for their confinement. What is amazing is that there were so few actual disasters.

The answer must be looked at from two angles—the immediate and the long-term. Meanwhile those concerned in the problem must stop blaming each other: the hospital criticising the G.P.s, the G.P. finding fault with the public-health clinics, and so on. The immediate answer is probably just that which you dislike so much—the early discharge of mothers to create more hospital beds. Having experience of this, I find it less objectionable than some of the other possibilities. The chief stumbling-block appears to be the Central Midwives Board whose regulations do not allow such early discharge cases to be counted in the teaching total. And here, you see, I am falling into the very trap I warned of—blaming others.

As a matter of urgency a senior and respected obstetrician should be appointed "chief of obstetric care" with powers to allocate patients to any hospital he chooses—teaching or otherwise. At the same time a specially convened committee could seek the ultimate solution.

London, W.12. STUART CARNE.

SIR,—You rightly draw attention to what is without a doubt a disgrace to our maternity services. My colleagues in general practice who have to deal with this problem must find the "emergency admission" procedure unsatisfactory to all concerned, most of all to the patient.

The solution does not, however, lie in the immediate provision of 200–300 extra maternity beds and their staffing. This would take months or years in any case, even if the staff were available, which is not forseeable at the moment. Family doctors, particularly those who are obstetricians, can help a great deal by improving the proper use of existing maternity beds by encouraging home confinement unless it is contraindicated; ensuring hospital booking for those who really need it; and adequate follow-up of pregnant women. Only thus will maternity beds be used to their greatest advantage. The responsibility of the family doctor does not end when he has given a pregnant woman a letter to an antenatal clinic and instructed her to start telephoning round London for a booking.

Let us now start an overdue searching of our consciences regarding our obligations towards the generation of the future and put an end to the present disgusting situation. The excellent help we receive from the E.B.S. is being grossly abused. It is mostly our own fault.

London, N.W.2. D. S. NACHSHEN.

SIR,—Leading articles illuminating the obscurer byways of medicine or even only surveying the pay and conditions of service of doctors rarely fail to stimulate lively correspondence from your readers. So far your comment of Oct. 14 on the failure of the London maternity service, an important part of a National Health Service that in all costs the public more than £2 million daily, has not induced any response. The subject may not be of interest, but certainly it is of importance.

Is your suggestion for more hospital beds the appropriate one? The higher intellectual endowment that is now required for nurse training, with a correspondingly diminished field of recruitment, the increasing competition from other fields of

employment, the earlier age of marriage, and the increasing disinclination of women to accept the hours and conditions of employment that hospitals demand, are some reasons for making it unlikely that it will be possible to staff additional hospital beds. In the future our reservoir of nursing skill will be among married women, with family responsibilities and available only for part-time non-residential work, whose services can be utilised most usefully in the homes of the patients. There is an encouraging tendency on the part of those concerned with the planning of our hospital service to advance from the position of deriding these considerations to merely discounting them.

The principal means of dealing with an increasing number of normal births will be confinement at home, conducted by domiciliary midwives most of whom will be married; adequate housing conditions and domestic help are prerequisites. The links between an adequate medical service and satisfactory environmental conditions, including housing, are indissoluble; and the planners would be well advised to realise that there are many health problems whose solution lies outside the clinical limits of the National Health Service.

Can your explanation be accepted that a situation that would not be tolerated in most parts of the country escapes general notice in London because the victims of the inadequate service are often immigrants, unmarried mothers, or the dim and feckless? Is it not because there is no-one to complain to? Members of boards of governors and regional hospital boards combine distinction with anonymity as far as the public are concerned, and at least the anonymity is shared by members of hospital management committees. Where the local health authority plays only a small part in the provision of maternity services the outraged patient is powerless.

Surely the answer is to have lively local health authorities, willing to ensure that the inhabitants of their areas are catered for adequately; and a local authority will only be lively when its elected members and its officers are constantly within reach of a population that knows them, and where to find them. This proximity provides a constant stimulus to purveyors of a defective service to have it remedied with the minimum of delay, and preferably before the next municipal elections if the members have their way. These considerations surely are topical in the Metropolis today.

Health Offices,
Wolverhampton. J. F. GALLOWAY.

## THE DANGER OF FOWLER'S POSITION

SIR,—Dr. Simpson and his colleagues (Oct. 21) confirm the general belief that the action of anæsthetics on the brain is completely reversible: barring accidents, anæsthesia, even in frail old patients, leaves no trace of damage in the nervous system. They thus remove the suspicion raised by Dr. Bedford [1] that it may have adverse cerebral effects on old people, and they give good reasons for reversing his opinion that old people should be subjected to operation only in "unequivocally necessary cases." They found, in fact, that these patients were often greatly benefited by operation and should be operated on, not less, but more often than at present. Their evidence is incontrovertible, and it seems to me of utmost importance to determine why the results of their investigation differ so markedly from those of Bedford's, which was equally well founded and made only a few years earlier in the same city.

Bedford found that of 251 elderly patients who were operated on between 1949 and 1954, no less than 18, all of whom were of normal or high intelligence up to the moment of operation, were afterwards grossly and permanently demented. Simpson, in 741 old patients undergoing operations in 1959, found not a single such case.

Simpson and his colleagues list several factors to explain this remarkable discrepancy, all of which no doubt played a part. Amongst them, however, is one that seems to me crucial and needing careful study—"realisation of the dangers of Fowler's position." If my information is correct, in Bedford's series Fowler's position was used routinely after operation: in Simpson's it was not.

Patients propped up in bed after operation not uncommonly develop "shock", with pallor, sweating, and sometimes loss of consciousness. This may occur in patients in whom it is least expected and after they have been upright several hours. Occasionally it is soon or instantly fatal, and no explanation of the death is found at necropsy. I have suggested [2] that this form of "shock" may often be nothing other than a common fainting attack, which, in a subject who is prevented from falling into the horizontal position, may result in severe stagnation or even complete arrest of the cerebral blood-flow. The brain is thus in the same danger as if the patient's heart had stopped beating, and this, I think, may have been the cause of the dementia in some of Bedford's patients. It is noteworthy that he described their state as "strikingly similar to that of young people surviving several minutes of cardiac arrest".

Surgeons are loth to abandon Fowler's position, because they believe it helps to prevent postoperative "chests". But Brock [3] has said that this is not so and that the patient can best clear his lungs lying down on his side and turned a little over on to his face.

Dr. Simpson's exemplary study should be repeated in some of the many hospitals that continue in the routine use of Fowler's position.

St. Thomas's Hospital,
London, S.E.1. J. G. BOURNE.

## ELECTIVE SURGERY ON OLD PEOPLE

SIR,—I was interested in the paper by Dr. Simpson and his colleagues (Oct. 21), who suggest that with good anæsthesia the elderly should not be deprived of the benefits of elective surgery. For me, the only disappointment in their paper was the omission of any proper consideration of the psychiatric aspects of their patients. I suggest that had more attention been given to these aspects, many of the 89 patients who came into the groups "patients living 'limited and much limited' existence after surgery" would either not have had their operations or would have been helped by psychiatric treatment before or after surgery.

Of the 3 examples given of patients in this group it seems likely that all would have benefited by treatment of their depression. But what is perhaps more important, patients like the arthritic lady of 72 might not have been operated upon. This lady's depression seems to have become evident after the relief of her backache.

Depression, particularly in the elderly, is frequently expressed in bodily symptoms. In particular, mild organic symptoms are exaggerated and elaborated. If these organic symptoms are removed, then the depressive feelings may become more evident to the patient and his doctor.

In some instances the very care and attention given in hospital may tempt them to allow their depression to come to the surface and not be hidden behind symptoms of organic illness. If this depression is not recognised and treated, it may deepen, or it may again be expressed through bodily symptoms. If the depression remains hidden it may find expression in complaints about the operation.

Early dementia and depression may mimic each other, and perhaps some of the cases of dementia described in previous papers on surgery in old age may in fact have been suffering from depression.

Another aspect of the treatment of the elderly which should be taken into consideration is the bad effect of moving from

1. Bedford, P. D. *Lancet*, 1955, ii, 259.
2. Bourne, J. G. *ibid.* 1957, ii, 499.
3. Brock, R. C. *Guy's Hosp. Rep.* 1936, **86**, 191.

familiar to unfamiliar surroundings. They are less adaptable, partly because of failure of their special senses, and it is often wise to familiarise them with hospital surroundings before operation and to discuss with them other changes they may experience—for example, that both their eyes will be covered after cataract extraction.

As is well known, old people often eat poorly, and vitamin supplements may decrease the incidence of post-operative confusional states.

If, as I believe, some of the failures in the series of Simpson et al. may be ascribed to insufficient consideration of their psychiatric state, then the conclusion that elective surgery in old age is usually beneficial is founded on yet firmer evidence.

University College Hospital
(St. Pancras Hospital),
London, N.W.1. EMANUEL LEWIS.

## DOCTORS FOR THE FORCES

SIR,—If there is a genuine shortage of Service medical officers—rather than an apparent one created by the previously untrammelled operation of Parkinson's law—perhaps this will induce those responsible to inaugurate a Combined Services medical service. The saving in manpower would be considerable. The objections and difficulties have been shown to be largely fictitious by the experience of a number of specialised units during the 1939–45 war.

Department of Neurology,
The Radcliffe Infirmary,
Oxford. C. W. M. WHITTY.

## THE DUMPING SYNDROME

SIR,—Mr. Wheeldon (Oct. 7) takes exception to the use of the word fat in our paper of Sept. 23 to describe the foods given.

In offering our explanation of the dumping attack, we stated: " The removal or bypassing of the normal gastric emptying mechanism allows fatty and/or sweet foods to pass through into the upper intestine . . . This rapidly produces striking peripheral vasodilatation." " Fatty and/or sweet foods " is a broad term intended to cover all the foods we had used up to date. The validity of our theory does not depend on the exact nature of the foods taken to reproduce the dumping attack. It was for this reason that, in our conclusion, we omitted any reference to particular foods.

The following case shows that an attack of dumping can follow a normal meal and that peripheral vasodilatation and a fall in blood-pressure are precisely similar to those induced by particular foods:

A man of 58 underwent partial gastrectomy for chronic gastric ulcer in 1956. He had no attacks of dumping for 5½ years. Attacks of dumping then began and were still present 2 months later when he was seen in the outpatient department. He stated that the attacks came on after nearly every meal. They were not connected with any particular food but were worse after hot foods. The symptoms in these attacks were severe and classical. On many occasions, he stated, on rising from the table immediately after his evening meal, the light-headedness, palpitation, and weakness were such that he had to go to bed. He found it necessary to climb the stairs on " all fours " because he felt he was in danger of falling. These symptoms, which he had experienced on standing, were completely relieved by lying in bed for 15 minutes.

He was admitted for investigation on Oct. 2, 1961. Blood-pressure on admission was 205/110 mm. Hg. Pulse 78 beats per min. Hæmoglobin 88%. The patient slowly and willingly walked up and down thirty steps and then up the same steps again. At the end of this exercise his blood-pressure was still 205/110. The patient was symptom-free except for slight tightness in his calf muscles. He was given an evening meal of hot soup, cold meat and salad, followed by a cup of hot tea with milk and sugar. On standing immediately after this meal and without exercise, the dumping attack came on and his blood-pressure fell to 180/100. The plethysmograph recording, taken at a later date on the second toe when he had had a similar meal, showed that vasodilatation had reached a peak before he had finished the soup. With rest in bed for a week, the attacks of dumping disappeared. He was again given a plate of soup, meat and salad, and hot tea with milk and sugar. On standing immediately after this, there was no attack of dumping and no fall in blood-pressure.

We feel that rest in bed improved the patient's cardio-vascular state, enabling him to compensate better for peripheral vasodilatation.

Manchester. H. T. COX.

## POSTNATAL EXERCISES

SIR,—Your note of Oct. 7 about the booklet planned by the Obstetric Association of Chartered Physiotherapists asked if two exercises—namely, raising both legs and slowly lowering them in the supine position, and " bicycling "—really should be avoided in the postnatal period. As Mrs. Williams and Miss Phillips made plain last week, they certainly should be, for though they may help to reduce flabbiness of the abdominal muscles they frequently cause pain in the back because the patient often grossly arches her lumbar spine to get the movement going. Backache starting in pregnancy and continuing long after the baby is born is such a frequent problem and such an uncomfortable symptom that nothing should be done which can possibly make it worse. Unfortunately few women directly complain of it, though questioning will reveal that its incidence in the puerperium is high. The other exercises recommended in the booklet do not strain the back and yet are just as good in restoring muscle tone, and what is perhaps more important restoring postural reflexes. The balanced activity of opposing sets of muscles is much more to be desired than overactivity of only one group. Progression from the mild exercises advocated in this booklet to more strenuous ones should be most carefully supervised.

The whole subject of postnatal exercises needs critical examination to make sure that they are not doing more harm than good. This booklet is definitely a step in the right direction, well away from exercises more suited to an athlete in full training than a woman who has just given birth to a baby.

St. Thomas's Hospital,
London, S.E.1. PHILIP RHODES.

## ANTICOAGULANTS IN ACUTE MYOCARDIAL INFARCTION

SIR,—Dr. Hilden and colleagues (Oct. 7) have misinterpreted my comments (Aug. 19) on their paper. My main contention was that although their trial was no worse than many that have been reported to favour the use of short-term anticoagulants in mycoardial infarction, where a report is in conflict with the majority opinion it must be able to satisfy reasonable criticism.

My first point concerned the design of the investigation which does not satisfy the ideal conditions for a therapeutic trial, and I cannot agree that it satisfies all the requirements I mentioned. Professor Holten (Sept. 23) and Dr. Deutsch (Sept. 9) have already questioned the randomised nature of the trial. Indeed, Professor Holten has shown that the results have, in fact, been misinterpreted and favour the administration of anticoagulants—at least in the first 48 hours.

It is doubtful whether anticoagulant treatment based on a combination of subcutaneous heparin and dicoumarol is

up-to-date therapy. I agree that the action of heparin given subcutaneously may be sustained, Hilden et al. produced no data in the form of clotting-time control to show that it was effective in their cases. Subcutaneous heparin is more unpredictable in action and potentially dangerous than intravenous heparin. The drawback to dicoumarol in its slow action in a disease with a high mortality in the first few days is obvious.

I did not, in fact, say that not enough dicoumarol had been given, although this is probably true. My main point, which Hilden et al. passed without comment, was that their results cannot be related to treatment in Britain and the United States where laboratory control is based on the Quick prothrombin time, which gives a greater reduction of coagulability than the P & P test at therapeutic ranges, with satisfactory thromboplastin extracts. I did not say either that a short-term trial of anticoagulant therapy in acute myocardial infarction would be impossible in Britain. I said the weight of medical opinion was such that it would be physically impossible to perform such a trial involving large numbers of untreated patients in the majority of hospitals in Britain.

The paper by Hilden et al. will have served a useful purpose if it emphasises that results of anticoagulant treatment are only worth while where the drugs are administered wisely and effectively. Where scrutiny of results such as these shows that benefit is not being achieved, or is very limited (if Professor Holten's figures are substituted), it is necessary to look for a cause.

Withington Hospital,
West Didsbury,
Manchester.

L. POLLER.

## TRANSFORMATION OF THE SMALL LYMPHOCYTE IN CULTURE

SIR,—In his preliminary communication of Oct. 14, Dr. Delorme reports that the infusion of isogenic rat lymphocytes plays some part in marrow regeneration after severe irradiation, although it is not yet certain that it is the lymphocyte which is the sole agent of repopulation. While many workers believe that the small lymphocyte [1] is merely the final stage of the series and is incapable of multiplication, Yoffey and his fellow workers [2] suggest that the small lymphocyte is in fact a resting form of a primitive mesenchymal cell. Bearing in mind that 95% of the cells used by Delorme were small lymphocytes, it may be of interest to mention work in progress in this laboratory.

Using a modification of the technique of Cassen et al.,[3] cells are obtained from human blood and then cultured in the presence of a mitosis-stimulating agent. Initially, the culture comprises cells which are approximately 84% small lymphocytes, 13% medium and large lymphocytes, 3% granulocytes, and less than 0·1% monocytes. After about 48 hours most of the cells are larger and of a more primitive appearance than any of the original mononuclear cells. During the first 24 hours no mitoses are present, and only 6% of cells go into mitosis in the next 24 hours; thereafter the number of cells entering mitosis rises and it may reach 40% between the fourth and fifth days. At the end of the third day, only a few cells are recognisable as being of lymphoid origin. The drop in the total count has never exceeded 25% and this loss is soon recovered. Thus it may be seen that the dominant cell type alters before a significant number of mitoses has occurred, and the change is not due solely to cell death in the small lymphocyte component.

Such results suggest that at least some of the small lymphocytes are capable of changing into a larger cell which has the power to divide.

Department of Hæmatology,
St. George's Hospital,
London, S.W.1.

KELVIN CARSTAIRS.

1. Trowell, O. A. *Internat. Rev. Cytol.* 1958, p. 285.
2. Yoffey, J. M., Courtice, F. C. Lymphatics, Lymph and Lymphoid Tissue; p. 430, London, 1956.
3. Cassen, B., Hitt, J., Hayes, F. M. *J. Lab. clin. Med.* 1958, **52**, 778.

## ADVERTISEMENTS FOR HEALTH

SIR,—Our attention has been drawn to the letter from a prominent advertising agent, Mr. R. A. Bevan, in your issue of Oct. 14, which ends with this sentence: "What I and most of my friends in advertising are anxious to avoid is a series of witch hunts such as are proposed by Mr. Francis Noel-Baker and the Advertising Enquiry Council on subjects on which there appears to be no finality of scientific opinion."

As an independent consumer organisation in which the medical profession is well represented, we have naturally often been asked to consider claims made in advertisements of medical and paramedical products. Where we consider it necessary, we make representations to Government departments and other bodies concerned, and we hope shortly to publish a detailed report on the whole subject of medical advertising to the public. This will be in the same series as our report on advertising by brewers and distillers, "Advertising Alcohol", which was published last October, and a report now in preparation on advertising by tobacco interests.

Presumably these activities are Mr. Bevan's "witch hunts". We propose to continue with them and also, incidentally, to continue to challenge dogmatic statements by advertisers "on subjects on which there appears to be no finality of scientific opinion".

FRANCIS NOEL-BAKER,
Chairman, Executive Committee,
Advertising Inquiry Council.

London, S.W.10.

SIR,—The correspondence following Dr. Mullins' article of Sept. 16 has been largely critical and in the main from those with declared interests, but I believe there is a very large body of support for the views she put forward, and considerable disapproval for the methods used in advertisements which affect the public health, whether directed to the public or to the medical profession. A crucial sentence in Dr. Mullins' paper has been ignored by her critics: "What is causing widespread concern, however, is the increasing use of 'persuasive' methods, whose aim is to reduce the consumer's ability to choose rationally." Many of us object strongly to these techniques.

The constant repetition and suggestion that sells detergents may do little harm, since Brand A and Brand B wash just as white as each other, and it doesn't matter very much if they don't, but harm *is* done when adolescents acquire potentially dangerous habits, sick people are led to try unproven remedies, the poor and aged spend money unnecessarily, and doctors prescribe preparations of uncertain value. The profession has no more immunity than the rest of the population against persuasive methods designed to influence selection, and indeed needs to be even more on guard against them than the rest of the community. Most medical men are grateful to the research organisations of pharmaceutical firms, and to the highly developed information services which they provide, but many are bitterly resentful of the tricks of pressure salesmanship.

Single truths do not necessarily add up to the whole truth. Journalists, advocates, politicians, and advertising agents are all well aware that by judicious selection the same set of truths can be made to support opposing views. Mr. Graves (Oct. 21) is doubtless factually correct when he works out the cost of 'Vitavel' syrup, but he ignores the fact that the housewife cannot buy it at the price he quotes, and he introduces other factors which confuse the issue: or does he imply that because the syrup contains vitamins A and B it will be possible to buy less bread and butter? His statements may be true, but you, Sir, drew attention to the retail price in your footnote.

Mr. Spencer Gore (Oct. 14) claims that his company "has

been at pains to ensure that our advertisements do not have misleading implications". This I would accept, but nevertheless it is my experience that many of the public *do* believe that the more "slimming food" they eat, the slimmer they will get, and this is the unfortunate result of the factually correct advertisements.

I must support Dr. Mullins in her reply to Professor Yudkin (Oct. 7). By his own findings the effect of any weight-reducing regime depends on its total calorie content, and to reduce the calories derived from carbohydrate at the cost of an increase in calories derived from fat will achieve nothing, unless the advice to the patient is suitably modified.

The original article was not primarily concerned with slimming foods, however, and it would be a pity if the arguments it raised become lost in a mess of starch-reduced foods. There is an enormous mass of advertising designed to influence habits, which has repercussions on health and thereby becomes of urgent and legitimate interest to the medical profession. Much of this advertising is to promote the use of tobacco, of alcohol, and of foodstuffs or food supplements. In addition we ought to be critical of a good deal of the commercial advertising which is directed to us, and emphasise to the drug firms that, although we value and depend on their information services, we deplore advertising techniques which are better suited to the gimmicks of an opulent society than to matters of health, life, and death.

Cheam, Surrey. ALEXANDER KAHAN.

## "THE INDUSTRY IT DESERVES?"

SIR,—As far as I know, we are the only general-practitioner group whose reports are published regularly, and so I can only assume that the criticisms of your correspondent (Oct. 14, p. 869) are directed against our work. The statement that the "ratio of favourable to unfavourable trial results (is) about ten to one" is certainly untrue for our group.

Among published reports of clinical trials, no matter where they are conducted, there is always a much higher proportion of successful results compared to unsuccessful ones. This is largely due to editors' reluctance to publish a large number of negative reports. Very often negative reports concern drugs which are subsequently abandoned, and never introduced to the general medical public, as a direct consequence of unfavourable clinical trials. Indeed, this is the very purpose of such trials. There can, therefore, be very little inclination on the part of editors, in view of overcrowding of their journals, to publish reports on drugs of no interest to the profession. This fact alone upsets the balance between successful and unsuccessful reports.

To appreciate the results of any clinical trial, it is necessary to define more clearly the terms "successful" and "unsuccessful". Not many new drugs are entirely without therapeutic action, although they may or may not be superior to older drugs. The demonstration that the drug concerned has the action claimed for it might be termed a "successful" result. Nevertheless, the drug may not be as effective as other drugs already available, but that does not entirely condemn it. If a trial demonstrates that only a small proportion of patients respond better to the new drug than to other remedies, then it will still have a place in treatment. Alternatively, a therapeutically inferior drug may become the drug of choice in general practice, because of fewer side-effects, or because it can be taken in a way that will not interfere with the patient's everyday life. To suggest that the pharmacological action of a drug in hospital is no different from its action in general practice is to ignore the problems of treatment in general practice. Can it be said that the "pharmacological action" of a ganglion-blocking drug is the same in the artificial conditions of a hospital bed as for the man running to catch his train in the morning? Clearly, the earlier ganglion-blocking drugs were an excellent treatment for hypertension for the patient in hospital, but the patient still has his hypertension when he returns to normal life, and if he faints on his way to work every morning, then he will not continue with the treatment. Thus, an alternative drug which does not produce this incapacitating side-effect becomes the drug of choice in general practice. This is a clear demonstration of the gulf which so often exists between institutional and domiciliary therapeutics.

To date, this group has completed 54 clinical trials on drugs with particular applications in general practice. I have attempted to put the results into four groups:

| | |
|---|---|
| Drugs concluded to be effective, no comparison made to other drugs | 2 |
| New drug better than other drugs | 12 |
| New drug as good as other drugs, but with no particular advantage | 18 |
| New drug not as good as other drugs, but may or may not have application to some patients | 22 |

Of the drugs in the first category, both are available; in the second category all but 1 are available; in the third and fourth categories all but 7 drugs in each are available. To date, we have published 15 reports,[1] and if these are similarly classified the proportions are as follows:

| | |
|---|---|
| Effective, no comparison | 2 |
| New drug better than other drugs | 4 |
| New drug as good as other drugs | 5 |
| New drug not as good as other drugs | 4 |

If we exclude from these trials those drugs which have not been made available, and allocate the remainder to either "successful" or "unsuccessful" results (this may be achieved by adding the first two groups and dividing the third group equally between the second and fourth groups), the proportions are as follows:

| | |
|---|---|
| Successful trials undertaken | 19·5 (published 8·5) |
| Unsuccessful trials undertaken | 20·5 (published 6·5) |

I admit that this does show a very slight favour in the direction of the successful results, but the ratio of 8·5 : 6·5 for published results does not approach anywhere near the figure suggested by your correspondent.

The General Practitioner Research Group, Twickenham. DAVID WHEATLEY.

SIR,—Referring to your anonymous correspondent's Point of View, I should like to comment as a doctor working in an independent research centre, where quite recently we have been joined by a group of like-thinking doctors, for the purpose of assessing drugs in general practice.

Much of what was said makes excellent sense, especially the extension of the Cohen (or similarly constituted) committee's functions and publication of their decisions. I find it hard, however, to reconcile two of the statements made: ". . . most of the so-called prestige products are not profitable, either to develop or to sell" and "Pharmaceutical companies undertaking original research and development, and producing worthwhile products would prosper". All companies want prestige, but the present-day evidence does not indicate that any particular firm is constantly producing "winners", and it follows that progress would soon cease under such another nationalisation.

With regard to the "other" drugs, why should we scoff? What parent will deny the ease of getting a child to take soluble aspirin instead of aspirin which remains in the glass, is taken last from the spoon, and spat out with tears? What ambulant bronchitic would not prefer to carry in his pocket a small dropper bottle, instead of the larger sticky bottle of codeine linctus? What patient would not prefer to take one capsule of a long-acting preparation night and morning instead of six tablets 4-hourly? Let us be realistic and occasionally remember the *patient*. Let us accept the palatable, not unpalatable, remedy but keep an eye on the cost. Where the increase in cost is out of proportion to the benefit for the patient, let us refuse to prescribe and hope that some other manufacturer will repeat the preparation at a reasonable price.

1. *Practitioner*, December, 1960, to September, 1961.

The vast majority of drugs are not " prestige " products, but when these highly active medicaments are required, I am sure they are prescribed. Of the other preparations, it must be remembered that the general practitioner wishes to ease his patients' symptoms (a point often ignored in hospital practice) and therefore he wishes for guidance on whether the new antitussive is more effective than codeine, whether the long-acting preparation really does release the drug effectively, and whether the combination is better than the original ingredient. The only way to discover this is by properly controlled double-blind trials in general practice with a statistician to help analyse the results. Hospital is not the place to carry out these essential assessments.

All trials *can* give incorrect results. Can anyone deny that cortisone is still better than aspirin in many cases of rheumatoid arthritis? " Built-in protection " is available using sequential procedures so that in 95 (or even 99) out of every 100 times the trial is repeated, the result will be correct, and the probability of the result being correct in an orthodox trial can easily be calculated and reported.

It may well be that too much personal payment passes into the hands of senior doctors, but this certainly is not so with the general practitioner. One reason for this practice is that the medical journals will usually publish readily the majority of contributions from a teaching hospital or " senior doctor ", so that there is little room left for minor efforts. The medical journals ought to realise that although the well-known have produced (and do produce) advances of great significance, it is surely as important to publish reports that may affect thousands of patients. Surely it is just as important to know that drug X is of no value or drug Y has a slight but definite advantage over the standard treatment, as it is to read of the fourth detected case of the ZZZ syndrome? It is of little use publishing long articles by senior doctors on the stature of the general practitioner and then to ignore the results he produces. For impartial and realistic decisions a committee of the Cohen type is in my opinion to be preferred to an editorial staff.

The question of payment is a common red herring which is of little importance in the properly controlled double-blind trial. Does the statistician object? I may add that in the trials we ourselves organise the general practitioner does not receive direct payment from the firm and is, in fact, unaware of its identity. It is agreed that uncontrolled trials are often useless, but who initiates these trials other than the pharmaceutical medical adviser? These clinical impressions are far commoner in the Continental and American literature, but which intelligent reader does not treat them as suspect?

Of greater importance, in my opinion, is the use of the placebo. The use of an inert negative control is surely against the conditions of employment under the National Health Service, even if not against medical ethics. The procedure is scientifically correct and used in animal experiments, but just as useful results are obtained in practice by the comparison with positive control substances, when the latter is a drug whose action is well known to all.

I would advocate (1) greater encouragement to the pharmaceutical industry, as it exists in Great Britain; (2) greater acceptance by this industry of the need for adequate toxicity tests [1]; (3) greater recognition of the general practitioner and the *patients he has to treat*; (4) greater numbers of controlled clinical trials of drugs in the field *in which they will be used*; (5) greater insight into the medical profession as a whole by those through whose hands information is spread by the printed word; and (6) greater sense of proportion to be exercised with regard to cost versus therapeutic value by all concerned, from Minister to patient, through hospital employee, pharmaceutical adviser, and general practitioner.

Nutritional Research Unit,
Huntingdon. PETER R. B. NOEL.

1. *Lancet*, Aug. 19, 1961, p. 422.

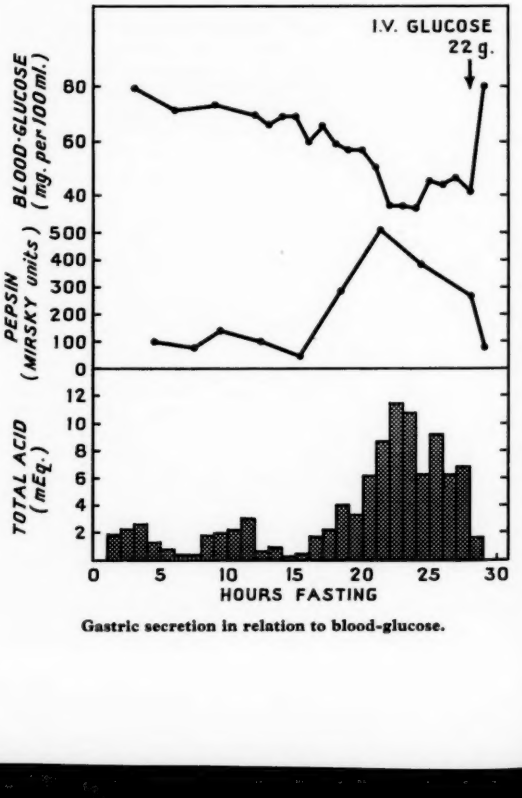
## GASTRIC SECRETION IN ORGANIC HYPERINSULINISM

SIR,—It is well known that peptic ulceration is found commonly in patients with alpha-cell tumours of the islet cells (Zollinger-Ellison syndrome) and in those with alpha-cell or beta-cell tumours who also suffer from multiple endocrine adenopathy.[1] The incidence of peptic ulceration, however, appears to be very *low* in patients with beta-cell tumours alone. There are records of close on 1000 such cases, associated with hyperinsulinism, in the literature, but in only 5 have we found associated peptic ulcer mentioned.[2–6] The low incidence may be apparent rather than real, for ulcers may not have been sought in these patients or not reported.

One might expect duodenal ulcer to be, if anything, *commoner* in patients with hyperinsulinism than in the general population, for hypoglycæmia is the main feature of the disease and is known to stimulate the secretion of vagal gastric juice in normal subjects. It is possible that, for some reason, hypoglycæmia does not stimulate gastric secretion in patients with organic hyperinsulinism. Smith and Cochran [7] investigated this point in one patient and found that the basal secretion of acid (and also gastric motility) were increased greatly during spontaneous hypoglycæmia.

We have recently studied gastric secretion during a prolonged fast in another patient with organic hyperinsulinism. He was a man of 57 with an islet-cell carcinoma (probably beta-cell) and multiple metastases in the liver. The stomach was emptied by aspiration every 15 minutes and blood (for estimation of true blood-glucose) was taken at intervals. The patient lay in bed and did not develop signs of hypoglycæmia. After 28 hours an injection of glucose (22 gm.) was given intravenously and secretion was collected for one more hour. The volume of each specimen of juice was measured. The total acid concentration was estimated by titration and the pepsin concentration

1. Gibson, J. B., Welbourn, R. B. *Post Grad. med. J.* 1960, **36**, 154.
2. Cunningham, L., Hawe, P., Evans, R. W. *Brit. J. Surg.* 1952, **39**, 319.
3. Janowitz, M. D., Crohn, B. B. *Gastroenterology*, 1951, **17**, 578.
4. Leffkowitz, M., Landau, B., Boss, J. H. *Gastroenterologia*, 1960, **93**, 157.
5. MacGregor, K. H. *Amer. J. Surg.* 1958, **96**, 98.
6. Ström, R. *Acta. chir. scand.* 1953, **104**, 252.
7. Smith, A. M., Cochran, L. B. *Lancet*, 1952, i, 289.




**Gastric secretion in relation to blood-glucose.**

(in 10 specimens) by a modification of the method of Fawcett.[8]

The results are shown in the accompanying figure. The secretion of acid and of pepsin started to increase when the blood-glucose fell to about 55 mg. per 100 ml. The secretion of both decreased abruptly within 15 minutes of the injection of glucose. It is clear that the spontaneous hypoglycæmia of organic hyperinsulinism stimulates the secretion of acid and of pepsin by the stomach. If the incidence of duodenal ulceration is lower in patients with this condition than in the general population, the cause is *not* unresponsiveness of the stomach to vagal stimuli.

Department of Surgery,
Queen's University of Belfast.

R. B. WELBOURN
J. T. WARD.

## INTRAMUSCULAR INJECTION

SIR,—In your annotation of Oct. 14, you refer to the hazards of superficial injections due to faulty technique. Another element of danger is the type of needle used.

The length of the needle for an intramuscular injection should be at least 2 in., and it is a disturbing fact that such needles are not always available—usually because needles become shortened after repeated sharpening.

But with the introduction of disposable needles, this situation should not arise, provided that the manufacturers are aware of the essential need for 2 in. needles.

St. Thomas's Hospital,
London, S.E.1.

F. TOOLE STOTT.

## RECRUITMENT AND TRAINING OF MENTAL NURSES

SIR,—Dr. O'Gorman (Sept. 23) makes some interesting points, but it is a pity that the tone of some of his comments does little to help create the atmosphere in which changes come about. As the husband of a one-time social worker, I often wished that social workers' duties ended at 5 P.M. If Dr. O'Gorman has found otherwise, then he may well be having a flood of applications for a post in his hospital!

As a psychiatric social worker, I can only agree, as would most of my colleagues I am sure, that the status of psychiatric nurses is not likely to be raised by making the training more like that of the general nurse. But surely revolutionary changes are already taking place in mental-nursing training in many psychiatric hospitals and within the present syllabus in spite of whatever faults it may have? It seems from Dr. O'Gorman's comments that this is not true of the hospitals for the mentally subnormal.

There is every possibility that in time the status of psychiatric nurses will equal, if not surpass, that of the general nurse, since they are being drawn more and more into the treatment of the patient. It would be a tragedy if the diversion of the psychiatric nurse from her primary function arose from rivalries about status, the basis for which lies more in the past than in the present or future.

I fully support the idea that the nurse should be included in social work activities and I hope that my colleagues will encourage this participation so that the nurses' knowledge may be used and extended by experience of the family and the community. I expect Dr. O'Gorman and I would disagree about the functions of social workers. In many ways the development of the nurses' activities has been thwarted by the attitude of the medical staff who have often created (sometimes with the help of senior nursing staff) such a military hierarchy in hospitals that the nurse's knowledge of the patient has been ignored to the detriment of her potential therapeutic functions.

As the hospital care for the mentally disordered changes, it may well be that a fresh look will have to be taken at the training of *all* the staff—doctors, nurses, social workers, and others. Change of any kind is always a challenge to attitudes and skills which have been developed in different circumstances; clashes of opinion are bound to occur. To take up the wrong battle position, however, may be just as damaging to one's cause as not being prepared to fight at all.

London School of Economics
and Political Science,
London, W.C.2.

R. C. WRIGHT.

## DOWN'S SYNDROME

SIR,—The fact that "everyone knows what mongolism implies" is surely one of the most compelling arguments for the use of a name for this syndrome which does not carry such implications. We are far more enlightened about this condition today than at any time "for over one hundred years".

The substitution of the term "Hansen's disease" for leprosy has been universally accepted and acclaimed—I feel a similar substitution for "mongolism" would be likewise. As regards the accuracy of the term, I would like to assure your correspondents of Oct. 21 that while my son has the features of Down's syndrome he is no more a "mongol" than they are.

A PARENT.

## ENDOMETRIOSIS

SIR,—Your leader of Sept. 23 draws the attention of physicians and gynæcologists in this country to the fact that effective medical treatment of endometriosis is now possible with norethynodrel. It may be of interest to your readers to have some further information on this subject.

*Dosage.*—It has now been reported by Kistner [1 2] that it is not necessary to give the high dosage of norethynodrel, originally recommended for long-term treatment. He has shown that a pseudo-pregnancy reaction may be produced equally effectively if treatment is begun early in the menstrual cycle with an initial dose of 2·5 mg. (rather than 10 mg. as used in the past), and the dose is gradually increased to 20 mg. daily, which is usually adequate for the maintenance of pseudo-pregnancy. This is in contrast with the much higher dosages which have sometimes been necessary to control breakthrough bleeding when this has occurred in patients receiving 40 mg. daily as previously given by Kistner or 30 mg. daily as given by Riva.[3] Details of the recommended dosage scheme based on Kistner's experience since March, 1960, have been published.[4] Apart from the resulting economy in the use of norethynodrel, the new dosage recommendations have lessened the side-effects such as nausea which sometimes accompanied high dosage.

*Duration of Treatment.*—You comment on the fact that Riva continued treatment beyond six months in only a few cases and that the (short-term) results were less satisfactory presumably due to more advanced disease. Kistner now has five years' experience, including more than 200 patients with proven endometriosis, and he advises that treatment should not be stopped before six months and in patients with extensive disease should be continued for nine to twelve months. In Kistner's most recent publication,[2] the recurrence-rates, in different groups of comparable patients, related to duration of treatment, were:

| | No. of Patients | Recurrence-rates Related to Duration of Treatment: 3 months | 4-6 months | 7-12 months |
|---|---|---|---|---|
| Endometriosis: no previous surgery | 53 | 4/10 | 2/27 | 1/16 |
| Recurrent | 35 | 1/6 | 1/19 | 0/10 |
| Endometriosis treated after conservative surgery | 22 | 0/16 | 0/3 | 0/3 |
| Total | 110 | 5/32 (15%) | 3/49 (6%) | 1/29 (3%) |

In view of the inferior long-term results following treatment of

8. Fawcett, J. K., *J. med. Lab. Technol.* 1951, **9**, 170.

1. Kistner, R. W. Personal communication, 1960.
2. Kistner, R. W. G. D. Searle & Co., Research Volume no. 54, p. 8.
3. Riva, H. L., Wilson, J. H., Kawasaki, D. M. *Amer. J. Obstet. Gynec.* 1961, **82**, 109.
4. 'Enavid' Reference Manual, no. 67, G. D. Searle & Co., February, 1961.

inadequate duration we advise against premature termination of treatment.

*Cyclic or Continuous Treatment.*—There is evidence [5 6] that the usual immediate effect of cyclic treatment is an exacerbation of the pain which usually accompanies menstruation in patients with endometriosis.

G. D. Searle & Co., Ltd., High Wycombe. G. R. VENNING Medical Director.

## A CHANGE OF NAME

SIR,—The Natural Childbirth Trust of Great Britain has changed its name to the National Childbirth Trust.

Since its beginning in 1956, the Trust's membership has greatly increased and the scope of its work has become much broader; it is now a truly national organisation.

In addition, the word " natural " has acquired a connotation, suggesting to many the rejection of analgesics and orthodox methods of helping women in labour when this is necessary. The chief aim of the Trust remains to make childbirth a happy and satisfying experience for all women, through education and the intelligent use of modern aids, thus contributing to the well-being of family life. It believes that this can best be achieved by full cooperation with the medical and nursing professions.

London, W.1. MARGARET BARLOW Vice-President.

## MEDICAL SERVICE COORDINATING COMMITTEES?

SIR,—In your issue of Aug. 26 Dr. J. R. Seale concludes that the operation of the National Health Service is mechanically unsound, while Dr. J. W. Todd quotes the opinion of historians on the profession's service to the public welfare in the two centuries before the 1946 Act.

In the 19th century the influences chiefly affecting this service to the public were (1) the Medical Act of 1858, which entrusted to the medical profession itself the task of regulating admission to the practice of medicine; (2) the active cooperation between philanthropy and the profession by which organisation of the service of the voluntary hospitals was left to a professional staff; and (3) the instructions to every local authority to appoint medical officers to organise measures to prevent the incidence and the spread of disease. In each of these activities the organisation of the profession's social service was left in its own hands.

Before the National Health Service, coordination of the three parts of this service—domestic, institutional, and preventive—was achieved by agreements between the members of their staffs. Admittedly, the coordination was imperfect: general practitioners did not always receive from doctors in hospitals (voluntary or municipal) either the assistance they needed for diagnosis or adequate information or advice when the patient left hospital. Nevertheless, cooperation was substantial, and much of it was contrived by means of medical societies set up in all but the smaller centres of population. At the meetings of these societies the family doctor and the hospital doctor met and exchanged views and information.

The N.H.S. has taken away much of the influence the profession previously had in the direction and control of its peculiar contribution to social welfare. The contribution of a hospital is no longer directed by the senior members of its medical staff sitting as a medical board; that of general practitioners is no longer governed by their own personal agreements. No longer are the medical boards free to select junior members of their staffs for promotion to higher grades of clinical responsibility.

These thefts from the profession's autonomy are the chief threat to its recruitment of the new members it will need. One of the most serious results of these thefts is that clinical clerks and dressers, house-physicians and house-surgeons, registrars and consultants will no longer sense their responsibility for the efficient working and reputation of one particular hospital and devote themselves accordingly. Under N.H.S. conditions the members of the hospital staff *belong* to no one hospital in particular: they are here today and may be anywhere tomorrow.

Can the profession's influence on the organisation of its own service be regained? Hope of this would be justified if the medical societies of the principal provincial cities would appoint medical service coordination committees which, in consultation with the councils of the Royal Colleges, would issue regular reports embodying their local findings and recommendations.

Faringdon, Berks. K. W. MONSARRAT.

## THE DISPOSAL OF INFECTED LINEN

SIR,—In condensing our article which you published on Sept. 9 we inadvertently left out a line, which has obviously caused a great deal of confusion.

The polyethylene bags are supplied in a continuous roll which is 15 in. wide. At intervals of 17 in. this is heat-sealed across its width, and perforated just above each sealed section, and the roll is "*sewn along one side with alginate thread*", as was stated in the summary but not in the main article.

Children's Hospital, Ladywood Road, Birmingham 16. K. B. ROGERS NOEL A. J. SLATER.

5. Holmstrom, E. G. *in* Proceedings of a Symposium on 19-Nor Progestational Steroids; p. 74. Chicago, 1957.
6. Weinberg, C. H. *in* Proceedings of a Symposium on Enovid; p. 20. Chicago, 1958.

# Parliament

### Smoking and Advertising

ON the adjournment on Oct. 18 Mr. FRANCIS NOEL-BAKER drew attention to the advertising campaigns of the tobacco manufacturers and, in particular, to their efforts to persuade young people and children to smoke cigarettes. As long ago as 1957, the Medical Research Council had stated that the risk for heavy smokers of cigarettes of developing cancer of the lung was nearly 40 times that for non-smokers. Medical opinion was equally dogmatic that chronic bronchitis was at least 6 times heavier among smokers than it was among people who did not smoke. Despite these 10-year-old warnings a recent survey in a county borough near London showed that over a quarter of grammar school boys and over a third of secondary modern school boys were smokers by the time they were 15, and were smoking over five cigarettes a week, and often more.

The two main groups selling cigarettes in Britain, Imperial Tobacco and Messrs. Gallaher Ltd., held between them 92·7% of the total trade in tobacco and cigarettes. In these conditions competition between various brands of cigarettes was not likely to be competition by price but competition by putting new brands on the market, by new sales gimmicks, and, above all, by intensified advertising campaigns. It was estimated that over £20 million a year was now spent on tobacco advertising. The tobacco companies would not spend this enormous sum unless they were convinced that it had a substantial effect in increasing their sales, and statistics showed a substantial increase in expenditure on tobacco and cigarette smoking by the population in general and by women and children and young people. These advertising campaigns constantly emphasised snobbery, vanity, and sex, and a large proportion appeared to be deliberately aimed at young people. Mr. Noel-Baker asked the Government to

issue a strong warning to the tobacco manufacturers telling them that unless they called off all advertising campaigns in the Press, on television, or on hoardings, aimed directly or indirectly at young people, the Government would take action to restrain them. He saw no reason why tobacco advertising should not be taken off the commercial television screen in the same way as the advertising of spirits had been. He would also be glad to see another stiff increase in taxation on cigarettes and a big dramatic increase in the efforts of the Government and of local authorities to warn schoolchildren and teenagers of the dangers of lung cancer and other diseases caused by cigarette smoking. The total of official money spent last year had been woefully inadequate, and many local authorities, doctors, and teachers were deeply disturbed that it was only a miserable trickle in the face of the millions spent for opposite purposes by the vested interests concerned.

Mr. NIALL MACPHERSON, parliamentary secretary to the Board of Trade, said that the Government in 1958 had asked local health authorities to make known the Medical Research Council's views. With few exceptions they had taken effective steps to do so, and most of them had concentrated their propaganda on schoolchildren and young people. No estimate of the cost of the publicity was available. Small-scale surveys supported the view that few if any of the public were now unaware of the risks of heavy smoking. The choice was theirs. The fact that some people misused their choice was no reason for damaging their freedom.

He agreed that there had been a considerable increase in tobacco advertising expenditure, but it had not been accompanied by any marked rise in the consumption of tobacco (133 million lb. for the first half of 1961, compared with 130 million lb. for the first half of 1960 and 124 million lb. for the first half of 1959). Much of the increase in advertising seemed to be due to new brands seeking to appeal to young people before they become committed to any particular brand. Firms were interested in enlisting new smokers of their cigarettes rather than just new smokers. It was not only the paid advertisement which stimulated a desire to smoke. It was the example of people around us, in the streets, in the train, on the village green. Advertising was the hallmark of a free society. It was playing a great part in raising the standard of living in this country. It would certainly have to play its part in our efforts to expand our export trade, and we ought to think carefully before we subjected any part of it to an unnecessary restriction. He doubted whether public opinion would support a prohibition on advertising tobacco in this country. In Sweden, where advertising was banned, tobacco consumption per head had not fallen.

What then, was to be done? He suggested that we should continue to do what we could to ensure that the public at large, and in particular parents, teachers, and those in daily contact with young people, were continually reminded of the facts and encouraged to ensure that those in their charge were made aware of the dangers of smoking. He hoped that the effect of the debate would be once more to remind all those who had a responsibility for young people that the Medical Research Council had reported that there had been a great increase in deaths from lung cancer in the past twenty-five years, and that the most reasonable interpretation of the increase was the smoking of tobacco, particularly in the form of cigarettes.

## QUESTION TIME

### Whitley Councils

Mr. R. W. MARSH asked the Minister of Health what new instructions he had given to his representatives on the health service Whitley councils in the light of Government policy on wages and salaries in the public service; and what limitations he had imposed on the right of arbitration in cases of disagreement between the two sides.—Mr. ENOCH POWELL replied: I have informed both sides of the Whitley councils that the same principles will be applied to the functioning of the health service machinery for determining pay as are being applied in the Civil Service. Mr. MARSH: Since the Minister of Health already has the right to reject any agreement within the Whitley council with which he disagrees, why does he refuse to permit the Whitley councils, management and staff sides, to negotiate operative dates of agreements? Mr. POWELL: It seems to me right that the same principle should be applied in all parts of the Government service.

Mr. KENNETH ROBINSON: Is the Minister aware that his unilateral action has gone further to destroy the confidence of National Health Service staffs in their negotiating machinery? Is he further aware that his action has had a serious effect on morale within the Service and on recruitment, particularly to those grades where there are serious staff shortages? Mr. POWELL: I am not aware of that, but I shall be seeing representatives of the Whitley Councils later this week and, naturally, I shall listen carefully to what they have to say.

### Chemists' Pay

Mr. ROBINSON asked the Minister what steps he was taking to ensure the dispensing of prescriptions in the event of the chemists giving notice to terminate their contracts and withdraw from the National Health Service.—Mr. POWELL replied: I must decline to answer the hon. Member's hypothetical question.

Sir HUGH LINSTEAD: I am sure the Minister will recognise that this cut in the chemists' remuneration is coming at a time when the number of prescriptions will already be reduced because of the 2*s.* charge. Can he tell the House how much he expects the saving effected by this cut to be? Mr. POWELL: Between £1$^1/_2$ million and £2 million per annum, but I should point out that the calculation of chemists' profits which is involved takes account of the known effect so far of the increased prescription charges.

### Drugs

Mr. D. L. LIPTON asked the Minister if he would make a statement on the steps he has taken to obtain cheaper drugs from abroad.—Mr. POWELL replied: Contracts have now been placed in accordance with my reply for the supply of five drugs for the hospital service. I estimate the total saving, before payment of royalties, at about £$^1/_2$ million in a full year.

Mr. ROBINSON: I appreciate that the Minister cannot be as forthcoming as he might be as he is about to be sued by one of the drug manufacturing companies, but will he say whether so far he is satisfied with the outcome of this experiment? Mr. POWELL: I have told the House that it has been found possible to place these contracts, and there is no question about the quality of the articles which are being obtained at advantageous prices. In due course royalties will either be negotiated or adjudicated.

### Health Service Expenditure

Mr. L. A. PAVITT asked the Minister what was the average amount per person spent within the National Health Service on health in Great Britain for the last three years to a convenient date.—Mr. POWELL replied: Including local health services and central administration, the figures to the nearest shilling are: £15 13*s.* in 1958-59, £16 15*s.* in 1959-60, and £18 10*s.* in 1960-61. Mr. PAVITT: Is the Minister aware that that £18 compares with £56 per head in the United States of America, and that if we wish to have parity with the United States we shall need to

spend another £235 million a year on the National Health Service? In view of the fact that in the year we lost 282½ million days in production because of ill-health, will the Minister not consider spending more on the National Health Service, especially on things other than the hospital service, to that end? Mr. POWELL: I do not think that international comparisons on this subject are much of an indication of the amount of service which is being given per head in the respective countries.

### Private Nursing-homes

Mr. N. N. DODDS asked the Minister if he had yet given consideration to the report on private nursing-homes sent to him on behalf of the National Corporation for the Care of Old People; and what action he contemplated taking to deal with the present situation.—Mr. POWELL replied: Yes, Sir: and the problems of registering authorities have recently been discussed with the local authority associations.

### Outside Contractors for Hospitals

Mr. ROBINSON asked the Minister what advice he had given or proposed to give to hospital authorities with regard to the placing of certain hospital services, such as catering and the cleaning of wards, in the hands of outside contractors; and what his policy is on this matter.—Mr. POWELL replied: Experiments are being made in the use of outside contractors. Pending the outcome no general policy has been recommended to hospital authorities.

Mr. ROBINSON: Would not the Minister agree that in principle it is desirable that these services should be kept within the control of the hospital authorities themselves? Are they not driven to these expedients only because they are unable to pay competitive wages and salaries to these grades of staff?—Mr. POWELL: Each service must be looked at on its merits. The guiding consideration must be economy and efficiency in the broadest sense, but I am not prejudiced in either direction and I shall certainly look at the outcome of these experiments carefully.

## Public Health

### Poliomyelitis in Hull

LAST Tuesday morning the cases of poliomyelitis in the Hull outbreak totalled 67—an increase of 21 on the total a week earlier.[1] The last of the special clinics opened for the mass administration of type-2 oral vaccine was being closed on Tuesday evening. At these clinics, each staffed by a State-registered nurse and by members of the public-health department, over 350,000 people had been immunised. The population of Hull is 302,000; and so at least 48,000 outsiders must have been vaccinated. It is expected that the response in Hull itself will prove to have fallen not far short of 100%.

*** We are grateful to Dr. Alexander Hutchison, the medical officer of health, for this information.—ED. L.

## Appointments

BOWE, J. C., M.D. Belf., F.R.C.P.E., D.P.H.; medical superintendent, Lingfield Hospital School for Epileptic Children, Surrey.
COLTART, W. D., M.B. Lond., F.R.C.S.: consultant orthopædic surgeon, Royal Masonic Hospital, London.
WATT, D. C., M.D., B.SC. Glasg., D.P.M.: consultant psychiatrist and medical director, St. John's Hospital, Stone, Aylesbury, and consultant psychiatrist, Aylesbury/High Wycombe department of psychological medicine.

**East Anglian Regional Hospital Board:**

MURLEY, A. H. G., M.B. Lond., F.R.C.S.: consultant orthopædic surgeon, Regional Hospital Board and United Cambridge Hospitals.
OSMAN, S. I., M.B. Cairo, M.R.C.P.E., D.P.M. & N.: registrar in psychiatry, Hellesdon Hospital.
PETROVSKAIA, BARBARA, M.B., PH.D. Edin., D.P.M.: senior registrar in psychiatry, St. Andrew's Hospital, Norwich.
TIWARY, PANCHANAN, M.B. Bihar, F.R.F.P.S., D.T.M. & H., D.C.H.: registrar in geriatrics, Ipswich and East Suffolk hospital group.

**Colonial Appointments:**

ESPITALIER-NOEL, J. A. L. F., M.B. N.U.I., M.R.C.O.G.: specialist obstetrician and gynæcologist, Mauritius.
KINGSLEY, MAURICE, M.R.C.S.: M.O., Tanganyika.
SHERRINGTON, A. M., B.M. Oxon.: pre-registration house-officer, Bahamas.

1. See *Lancet*, Oct. 21, 1961, p. 938.

## Notes and News

### MEANS OF IDENTIFICATION

THE Medical Defence Union and the Royal College of Nursing have published a joint memorandum suggesting safeguards against the risk of a surgeon operating on the wrong patient, side, limb, or digit. The Medical Defence Union has dealt with 28 such cases within two years, and there is clearly need for every surgical unit to review its present procedure.

*Operating on the wrong patient*

In a busy casualty department notes may be attached to the wrong patient, or a patient's marked clothing may be removed. In a surgical ward the position of beds may be changed on an operation day, or the ward may not be sent timely warning of changes in the theatre list. Confusion may also arise if two patients have the same name. To counter these hazards the memorandum suggests that all unconscious patients admitted through the casualty department and all patients going to the operating-theatre should have an identity disc or label attached to wrist or ankle bearing the name, initials, and hospital number, and that this labelling should be the responsibility of the casualty or ward sister. A surgeon should visit his patient in the ward beforehand, and examine the patient's records to make sure that the notes relate to that patient and that the entries are correct. The patient's name, initials, and hospital number should be recorded on the operation list, and copies should be displayed in the anæsthetic room and in the ward, as well as in the operating-theatre. Patients should be summoned to the theatre by name and number, and never as "the patient from such-and-such a ward".

*Operating on the wrong side or limb*

This accident is more often due to mistakes in the case-notes—e.g., "right" instead of "left"—or illegible writing. It may also happen when the entry on the operation-list has not been checked with the notes taken to the operating-theatre, where the wrong case-notes accompany the patient; where the wrong side or limb has been prepared, and where there is no routine procedure for marking the operation side.

It is suggested that the side on which the operation is to be performed should be indelibly marked before the patient reaches the theatre, and that the side should also be marked with a skin pencil on the patient's forehead. This should be the responsibility of the house-surgeon, and could usually be done on the evening before the operation. If it is discovered that this has not been done, the sister should inform the surgeon who is to operate, but should not make the marking herself. The word "right" and "left" should be written in full on the patient's notes and on the operation-list.

*Operating on the wrong digit*

This may be caused by any of the causes described above. An additional hazard is to refer to the fingers by number instead of by name, and it is suggested that fingers should always be described as thumb, index, middle, ring, and little fingers (and not as first, second, third, fourth and fifth). Toes should be described as hallux (big), second, third, fourth, and fifth (little).

To reach agreement on a site routine procedure, incorporating as far as possible these safeguards, a joint committee of medical and nursing staff, including the matron and a representative of the consultant surgical staff, should be set up in each hospital or group of hospitals.

### EMPIRE INTO COMMONWEALTH

MUCH of Sir George McRobert's work was done in India, and at his presidential address on Oct. 12 to the Royal Society of Tropical Medicine and Hygiene he recalled the little-known fact that the political emancipation of India was the eventual goal of British administration even a hundred years ago. By 1921 there were Indian and Burmese governors of major provinces, chief justices, vice-chancellors of universities, and Ministers, under whom Sir George and his colleagues worked in harmony.

The civil branch of the Indian Medical Service was largely responsible for introducing modern science into India, but its highest achievement was in education; by 1947 there were Indian professors in every branch of medicine and surgery. In medical education a dual system was worked, in which the licensed medical practitioners who had taken a course of three years were allowed to practise in permanently subordinate positions, though many of them became highly expert. In the higher grade were the full university graduates. This system led to jealousies, and it was ended after Independence. But in emerging countries, Sir George thought, there is so great a need for doctors or assistants, to carry out mass treatment, vaccination, and public-health programmes, that some form of dual system may still have a place.

Now, however, Britain can only advise, realising that the emerging countries are their own masters, and that requests for advice must come from them. The recent creation of the Department of Technical Cooperation and the Tropical Medicine Research Board under the Medical Research Council may be of great benefit if there is mutual trust and confidence between the emerging countries and Britain. But this depends very largely on political factors, and we in this country should not expect preferential consideration.

The popular idea of medical help usually envisages hospitals and curative services, even including provision of equipment for advanced surgery. But after peace and security the greatest needs are for the development of agriculture, irrigation, and primary education, and for the means to combat the common debilitating diseases: a compounder with a few shillings' worth of chloroquine and sulphonomides can be more useful than an expert with thousands of pounds worth of electronic equipment. Research is always necessary, and priority should go to research on nutrition and family limitation: the atomic bomb is not so dangerous as the atomic womb.

Though we should not embarrass the new countries with white elephants—gigantic hospitals, electron microscopes, and other specialised equipment—we can help in research if our own people can be given security of tenure and long-term prospects of employment in these countries. International cooperation and teams for special investigations have become essential to cope with modern problems, and they have already been provided for the work on the Kyasanur forest disease and for the Madras investigation of tuberculosis.

Sir George summed up by saying that much of the money from British sources should be spent on British-based research, and most of the remainder on health education. It should be administered with tact, sympathy, and a sense of proportion, and the education we offer to students and graduates from abroad must be of the highest quality.

## NEW PSYCHIATRIC UNIT AT BRISTOL

ON Sept. 30 Sir Philip Morris, vice-chancellor of Bristol University, opened John Cary House, which is a specialised admission unit for 24 patients of either sex. Accommodation is in comfortable rooms for 1–3 patients, and recreational space is generous; with a planned average stay of a month, admissions should number about 300 a year. An intensive social and occupational programme is planned, and nurses will take an active part both in history-taking and in home visits. Research at present in hand is devoted especially to study of the effects of treatment under controlled conditions: sound-proofed rooms will be used for conditioning and behaviour therapy. Students will have access to the unit.

## MEDICAL RESEARCH COUNCIL

THE Council has moved its offices to 20, Park Crescent, London, W.1. Designed by Nash, the crescent is at the north end of Portland Place, and this part of it was destroyed during the war. Though the new front exactly matches those of its neighbours, the interior has been built afresh for its purpose.

At the house-warming on Oct. 19, guests were received by Lord Shawcross, who lately took office as chairman of the Council, and Sir Harold Himsworth.

### University of London

On Monday, Nov. 13, Prof. A. V. Neale will give the first of five Heath Clark lectures on advancement of child health, when he will speak on child health—past and present. The subjects of his other lectures will be: Nov. 15, human reproduction; Nov. 21, epidemiological trends and achievements, with particular reference to tuberculosis; Nov. 23, juvenile rheumatism; Dec. 1, child health in its medical, educational, cultural, and humanistic aspects. All the lectures will be given at 5.30 P.M., at the London School of Hygiene and Tropical Medicine, Keppel Street, W.C.1.

### University of Manchester

Dr. P. J. Collard, who held the chair of bacteriology in the University College of Ibadan, Nigeria, has been appointed professor of bacteriology and director of the department of bacteriology and will take up his duties in Manchester in April, 1962.

Dr. Collard qualified from St. Bartholomew's Hospital, and after holding appointment as a house-physician at St. James's Hospital, Balham, he took the M.R.C.P. in 1943. He then became R.M.O. at Hurstwood Park E.M.S. Hospital. From 1945 to 1948 he served as medical registrar in pathology at the Westminster Hospital, and in 1950 he was appointed lecturer in bacteriology in Guy's Hospital, later becoming senior lecturer. He took up his present chair in 1954 and during 1959–60 he was dean of the faculty of medicine at Ibadan. He also holds appointments as honorary consulting bacteriologist in University College Hospital, Ibadan, and is consultant adviser on industrial microbiology to the Federal Institute of Industrial Research of the Nigerian Ministry of Commerce and Industry. He is at present carrying out an epidemiological survey in Northern Nigeria, measles vaccine trials, and an investigation of the biochemical lesion in the gut epithelium in shigellosis.

### University of Sheffield

Miss M. A. C. Jones has been appointed part-time clinical teacher in ophthalmic surgery, Mr. C. H. Talbot part-time clinical teacher in surgery, Dr. Malcolm Green part-time tutor in pharmacology and therapeutics, Mr. W. J. Lytle part-time director of postgraduate clinical studies and lecturer within the department of surgery, and Dr. J. G. McCrie honorary lecturer in the history of medicine.

### Royal College of Physicians of London

Prof. Sheila Sherlock will give a Bradshaw lecture on Thursday, Nov. 23, at 5 P.M. She will speak on jaundice. Dr. J. A. Fraser Roberts will give a Charles West lecture on Tuesday, Nov. 28, at 5 P.M. His subject will be genetic prognosis. Dr. K. D. Keele will give the third and fourth FitzPatrick lectures on Tuesday, Dec. 5, and Thursday, Dec. 7, at 8.30 P.M. He will speak on the evolution of clinical methods in medicine. All the lectures will take place at the college, Pall Mall East, S.W.1.

### Welsh National School of Medicine

Mr. G. E. Heard has been appointed senior lecturer in the surgical unit of the Welsh National School of Medicine at the Cardiff Royal Infirmary.

### Royal Australasian College of Physicians

At a meeting of the general body of fellows of the college held in Adelaide on Oct. 11 the following were admitted to fellowship:

*Under article 44:* Ewan Murray-Will (New South Wales); R. A. Willis (England).

On Oct. 9 the following were admitted to membership:

Kurt Aaron, J. H. Casey, R. Gordon (Queensland); R. B. Goldrick, R. W. Haber, L. B. Hardacre, C. I. Johnston, P. H. Miles, K. W. Perkins, M. C. Rozenberg (New South Wales); Helen Byrne, J. H. Coldbeck, B. S. Gilligan, F. W. Gurr, Priscilla Kincaid-Smith, A. Kucers, J. A. Mirams, W. B. Stephens (Victoria); M. W. Begg, D. E. Dunn, M. W. Miller, D. N. Phear (South Australia); P. M. Connor, S. S. Gubbay (Western Australia).
*Under article 37:* J. V. Hurley (Victoria).

### British Society for Immunology

A meeting of this society will be held on Nov. 17 and 18 at the Wellcome Building, 183, Euston Road, London, N.W.1. The programme will include a symposium on tissue antigens, when the chairman will be Dr. L. E. Glynn. Further particulars may be had from the meetings' secretary, Dr. R. G. White, bacteriology department, London Hospital, E.1.

### Royal College of Surgeons of Edinburgh

At the annual meeting of the college on Oct. 18 with Prof. John Bruce, the president, in the chair, the following officers were elected:

President, Prof. John Bruce; vice-presidents, Prof. Norman Dott, Prof. Bryan McFarland; secretary, Mr. J. A. Ross; treasurer, Mr. J. J. Mason Brown; president's council, Mr. David Band, Mr. J. R. Cameron, Dr. J. B. Dewar, Mr. I. L. Dick, Mr. E. L. Farquharson, Mr. A. J. C. Hamilton, Mr. J. N. J. Hartley, Prof. A. S. Johnstone, Dr. R. G. Macbeth, Dr. D. S. Middleton, Mr. R. L. Stewart, Mr. G. M. Sturrock, Mr. T. I. Wilson; representative on the general medical council, Mr. K. Paterson Brown; conservator of museum, Prof. E. C. Mekie; hon. librarian, Sir Walter Mercer.

The honorary fellowship was conferred on Sir Arthur Porritt, and the following were admitted to the fellowship:

George Abrami, Nazir Ahmed, D. L. Annetts, J. B. Arnot, A. M. Bain, D. T. C. Barber, Nagui Helmi Bedwani, Doreen A. Birks, Sudhansu Bimal Biswas, W. J. O. Box, C. T. M. Cameron, H. M. Chung, R. B. Conyngham, A. C. Cyrus, B. H. Dawson, J. C. De Villiers, Mohamed Ali Elwi, J. J. Enwright, Maureen F. Esmonde-White, R. N. Gale, Devikishan Karwa Gattulal, Fouad Hassan Ghali, Sankara Gopala Pillai, B. K. Gray, E. R. Griffiths, J. A. Hamilton, G. A. Hanks, Susan E. A. Hart, Shanmugam Kameswaran, Malwindar Want Kaur, Ullal Keshav Kini, Kais Kubba, Ariyasinghe Edmund Kulatilake, G. J. McCafferty, H. W. McFarlane, J. W. McIntosh, N. A. Matheson, Donald Mayor, Vijay Labhshankar Mehta, Prayagraj Mondal, Krishnan Parameswaran Nair, Arcot Jayaram Narendran, M. J. Notaras, J. C. Park, G. H. Parker, T. A. Piggot, R. W. Porter, G. J. Rice, W. M. Rigal, Guru Prasad Sarma, Amarendra Sen Gupta, Somendra Mohan Sengupta, Nanak Chand Singhal, F. S. Smith, J. S. S. Stewart, P. W. Stewart, David Stuart, J. N. Taylor, V. R. Tindall, Cedric Wannenburgh, A. K. Wyllie.

### United Leeds Hospitals Board of Governors

Sir Donald Kaberry, M.P., has been appointed chairman of this board in succession to Sir George Martin.

### Royal Medico-Psychological Association

A quarterly meeting of this Association will be held at 11, Chandos Street, London, W.1, on Nov. 14 and 15, under the presidency of Dr. William McCartan.

### Group for Representation of the Views of Clinical Psychiatrists

The constitution of this group has been amended and medical superintendents and directors are now eligible for membership. The present membership is over 200 senior psychiatrists. It will in future be known as the Society of Clinical Psychiatrists. The officers are: Dr. J. T. Hutchinson (chairman); Dr. M. F. Bethell (treasurer); and Dr. B. M. C. Gilsenan, Shenley Hospital, nr. St. Albans, Herts. (hon. secretary).

### Ministry of Education

Dr. A. F. Alford has retired from the Ministry after 23 years' service. Dr. C. B. Huss, senior medical officer, has succeeded him as deputy to Dr. P. Henderson, the Ministry's principal medical officer. Dr. G. M. Fleming has left the Ministry's service on his appointment as a senior medical officer at the Ministry of Health. Dr. Anne Guy and Dr. Esther E. Simpson, have been appointed medical officers at the Ministry.

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Surgeon Captain H. L. Cleave has been appointed honorary surgeon to the Queen in succession to Surgeon Captain W. J. M. Sadler.

On Nov. 18 and 19 at the Royal College of Surgeons, Lincoln's Inn Fields, London, W.C.2, the Faculty of Radiologists is to hold a postgraduate weekend course. Further particulars may be had from the secretary of the Faculty, 47, Lincoln's Inn Fields, W.C.2.

On Saturday, Nov. 4, at 2.30 P.M., at Queen Mary's Hospital, Roehampton, London, S.W.15, the Southern region of the Association of Clinical Biochemists is to hold a symposium on electrophoresis. The hon. secretary of the region is Mr. P. M. G. Broughton, Biochemistry Laboratory, St. John's Hospital, Chelmsford, Essex.

On Saturday, Nov. 11, the department of photogrammetry and surveying of University College London is to hold a symposium on photogrammetry in medicine and biology. Further particulars may be had from the secretary of the department at the college, Gower Street, W.C.1.

Mr. John Garnett has been appointed director of the Industrial Welfare Society.

The *University of Leeds Medical Journal* has ceased publication. The last issue appeared in May, 1961.

Mr. Ludwig Guttmann, director of the National Spinal Injuries Centre, Stoke Mandeville Hospital has been awarded the Werner Ruhemann plaque by the German Medical Association of Sport Medicine.

A semipermanent exhibition will be held at the Institute of Dermatology, Lisle Street, London, W.C.2, from Nov. 1 to 29, by Dr. E. J. Moynahan on the biology of the skin surface.

CORRIGENDUM: *Ice Arrest of the Heart.*—In Mr. Arkless's letter of Sept. 16, the second sentence should have ended ". . . that part which melts first has a *higher* concentration of salt than have the still frozen crystals."

## Diary of the Week

OCT. 29 TO NOV. 4

### Sunday, 29th

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, W.C.1
10.15 A.M. Mr. S. E. Birdsall: Common Ear, Nose, and Throat Conditions.

### Monday, 30th

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road, W.12
4 P.M. Dr. R. F. Mahler: Glycogen Storage Diseases.
UNIVERSITY COLLEGE LONDON, Gower Street, W.C.1
5 P.M. Prof. J. N. Davidson: Biosynthesis of Polynucleotides. (Second of two lectures.)
BRITISH POSTGRADUATE MEDICAL FEDERATION
5.30 P.M. (London School of Hygiene and Tropical Medicine, Keppel Street, W.C.1.) Prof. R. G. Harrison: Functional Aspects of the Vascularisation of Tissues.

### Tuesday, 31st

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
5.30 P.M. *Experimental Medicine and Therapeutics.* Dr. M. Hašek (Prague), Dr. M. Simonsen (Copenhagen), Dr. R. E. Billingham (Philadelphia): Transplantation.
INSTITUTE OF DERMATOLOGY, Lisle Street, W.C.2
5.30 P.M. Dr. W. K. Silvers (Philadelphia): Analysis and Implications of the Phenomenon of Pigment Spread in Guineapig Skin.
ST. MARY'S HOSPITAL MEDICAL SCHOOL, Paddington, W.2
5 P.M. Mr. A. M. Sutherland: Functional Uterine Hæmorrhage.
WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY, 91, Dean Street, W.1
5.30 P.M. Dr. G. F. Swann: Auto-tomography in Cerebral Pneumography.
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE, 28, Portland Place, W.1
5 P.M. Dr. Henry K. Beecher: Nonspecific Forces Surrounding Disease and the Treatment of Disease. (Bengué lecture.)

### Wednesday, 1st

POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P.M. Prof. D. A. K. Black: Gastro-intestinal Functions.
ROYAL SOCIETY OF MEDICINE
5.15 P.M. *History of Medicine.* Dr. Raymond Hierons, Prof. Alfred Meyer: Priority Questions Arising from Thomas Willis's Work on the Brain.
INSTITUTE OF DISEASES OF THE CHEST, Brompton, S.W.3
5 P.M. Dr. F. J. Prime: Pulmonary Lesions and Changes of Function in Chronic Bronchitis.
MIDLAND MEDICAL SOCIETY
8.30 P.M. (Birmingham Medical Institute, 36, Harborne Road, Birmingham, 15.) Dr. J. M. Malins: Diabetes.
MANCHESTER MEDICAL SOCIETY
4.30 P.M. (Medical School, University of Manchester.) Mr. Rodney Smith: Expanding Scope of Hepatic Surgery.

### Thursday, 2nd

UNIVERSITY OF LONDON
5 P.M. (1, Wimpole Street, W.1.) Mr. C. P. Wilson: Pharyngeal Diverticula, their Cause and Treatment. (Semon lecture.)
FELDBERG FOUNDATION LECTURE
5.30 P.M. (University College London.) Prof. Herbert Hensel (Marburg): Electrophysiology of Thermoreceptors.
BRITISH POSTGRADUATE MEDICAL FEDERATION
5.30 P.M. (London School of Hygiene and Tropical Medicine.) Prof. J. J. Pritchard: Bone Healing.
LIVERPOOL MEDICAL INSTITUTION, 114, Mount Pleasant, Liverpool, 3
8 P.M. Mr. W. M. Beattie, Dr. V. K. Summers, Dr. M. A. Stewart, Mr. A. M. Abrahams: Carcinoma of the Breast.
HONYMAN GILLESPIE LECTURES
5 P.M. (University New Buildings, Teviot Place, Edinburgh.) Dr. W. M. Court Brown: Contributions of Human Cytogenetics to the Study of Disease.
UNIVERSITY OF ST. ANDREWS
5 P.M. (Physiology Department, Queen's College, Dundee.) Prof. Martin Roth: Mental Illness in Old Age and General Problems of Psychiatry.

### Friday, 3rd

POSTGRADUATE MEDICAL SCHOOL OF LONDON
10 A.M. Mr. A. L. Eyre-Brook: Difficulties of Diagnosis in some Malignant Tumours of Bone.
ROYAL SOCIETY OF MEDICINE
10.30 A.M. *Otology.* Mr. T. A. Clarke: Deafness in Children. (Presidential address.)
2.30 P.M. *Laryngology.* Mr. N. Asherson: Vagaries of Dysphagia. (Presidential address.)
6 P.M. *Anæsthetics.* Dr. Robert Cope: Emergencies. (Presidential address.)
INSTITUTE OF LARYNGOLOGY AND OTOLOGY
3.30 P.M. Mr. D. F. N. Harrison: Sore Throat.